"THE EEG JOURNAL"

ELECTROENCEPHALOGRAPHY and CLINICAL NEUROPHYSIOLOGY

Official Organ of the International Federation of EEG Societies

This Journal was inaugurated in June, 1947 by the Executive Committee of the International E E G Organization at their first meeting in London Its purpose is threefold to provide an official organ for the various EEG Societies being established throughout the world, to bring together in one publication selected studies of merit in the growing field of neurophysiology as applied to the understanding of human behaviour, both normal and abnormal, and to foster international cooperation and understanding among scientists with these common interests

Studies of the electrical activity of the brain provide the central theme of this Journal Its scope however, is far broader, to include any aspect of the physiology of the nervous system or neuromuscular system which may contribute to progress in our understanding of the neural basis of behaviour Studies relating to disorders or diseases of the nervous system will be of particular though not exclusive interest.

Each Annual Volume will contain approximately 500 pages of scientific material This will appear in quarterly issues The text of each communication will be published in the English French or Spanish language Abstracts, not to exceed 1000 words will appear in English if the text is in French Authors are requested to submit manuscripts in the language of their choice for publication, preferably in English since the larger proportion of our readers are more familiar with this language Abstracts should be submitted in the language most familiar to the author to be translated by the editors when necessary

Manuscripts will receive prompt publication following their acceptance In most cases, the delay will not be more than 3 months As a rule authors will be given the privilege of withdrawing their manuscripts if they cannot be published within 6 months of their acceptance

Authors instructions for the preparation of manuscripts are given in the first issue of this Journal Papers should be concise with a brief Introduction, followed by Technique, Results Discussion or Interpretation and a Summary which may be the same as the Abstract if the author chooses Citations to literature should be by author and year, arranged in alphabetical order appearing at the end of the text Full references must be given as follows

HARVEY H N and SMITH J The Anatomical Basis of the Alpha Rhythm EEG Clin Neurophysiol 1949 1 200-220

MANUSCRIPTS from the Americas the Pacific and Far East to Dr Herbert H Jasper, Editor
3801 University St Montreal 2, Canada

From the British Isles, Europe, Africa, Middle East and U S S R to Dr Grey W Walter, Co-Editor
The Burden Neurological Institute, Bristol England

SOCIETY PROCEEDINGS to Dr John R. Knott,
Psychopathic Hospital U of Iowa Iowa City Iowa

TECHNICAL NOTES
to Dr Geoffrey Parr 68 Compton Road London England
or Dr E J Baldes, The Mayo Clinic Rochester, Minn U S A.

SUBSCRIPTIONS and ADVERTISEMENTS
to Dr Robert S Schwab Managing Editor
Massachusetts General Hospital, Boston 14 Mass

Annual subscription rate is eight dollars ($8 00) payable in United States or Canadian currency A reduced price is given to subscriptions paid through E E G Societies

GRASS INSTRUMENT CO
101 OLD COLONY AVE
QUINCY MASS
PR3-0002

February 1, 1949

To the Editors and Readers of
The Journal of Electroencephalography and
Clinical Neurophysiology

We extend our congratulations to the Editors on the inauguration of this Journal devoted exclusively to Electroencephalography and Clinical Neurophysiology. This venture will provide an international facility for the exchange of information which deserves everyone's support, financial and otherwise, to guarantee the Journal's lasting success.

The Journal can count on the support of our organization which itself has devoted the last fourteen years exclusively to instrumentation of Electroencephalography and Electrophysiology for international use.

For us the Journal is a medium for advertising our products, for maintaining close customer relationships, and for contributing our ideas and information for the improvement of techniques which in the past had to be done by correspondence and discussion.

Very truly yours,

GRASS INSTRUMENT COMPANY

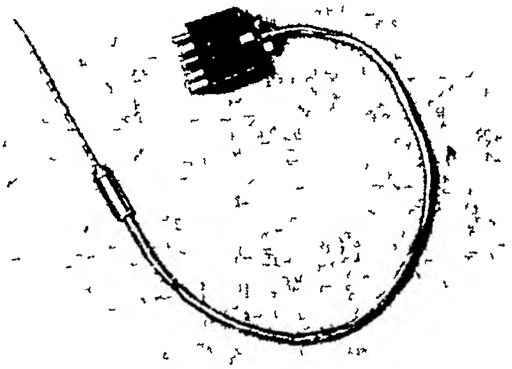
Albert M. Grass

Ellen R Grass

GRASS INSTRUMENT CO
101 OLD COLONY AVE
QUINCY MASS
PR3-000Z

S P E C I A L   D E V I C E S

During the years spent in the development of Electroencephalographs and Electrophysiological instruments, Grass Instrument Company has acquired the extensive facilities, the expert craftsmanship, and the engineering "know-how" needed to produce economically in quantity the special technical devices for this field. Below is a typical example of such a project.



Depth Electrode

Developed in conjunction with Dr. Frederic A. Gibbs of the University of Illinois.

The Electrode is used in the investigation of electrical activity at various depths in the brain during operation. It is a probe two millimeters in diameter with ten contacts. Can be sterilized in autoclave.

MAKERS OF ELECTROENCEPHALOGRAPHS AND ELECTROPHYSIOLOGICAL INSTRUMENTS SINCE 1935

SYMPOSIUM

PHYSIOLOGICAL BASIS OF EPILEPTIC DISCHARGE

Commission

Ralph W Gerard *Chairman*
Detlev Bronk
Earl Walker
Wilder Penfield

Speakers

Wilder Penfield
Herbert H Jasper
Warren McCulloch
Chester W Darrow
Detlev Bronk
K A C Elliott
James E P Toman
William G Lennox
Ralph W Gerard

ANNUAL MEETING

American Electroencephalographic Society
Atlantic City
June 1948

OPENING REMARKS

Ralph W Gerard, M D , Ph D
Department of Physiology, University of Chicago

I should like to take my prerogative as Chairman, to introduce the symposium along the lines of Dr Jasper's presidential address last night We were complaining to each other before that meeting, that the questions which had agitated the workers in this field in the pioneer days of long, long ago (all of fifteen years !) did not seem to be much in the forefront these days — not because they had been solved but because they had become neglected There has been a trend it seems to me, to look at records of the electrical activity of the brain, which constitute the main stock in trade of electroencephalographers, in the manner of the classical structural anatomists We find ourselves examining these wiggles, which constitute some sort of an entity structurally — they are long or short, frequent or slow sharp or round — rather than seeing them dynamically and functionally and remembering that they are but an index of processes and functions

I think the history of thought about convulsive or epileptic problems has shown the same trend, only fortunately in reverse, originally, the problems were mainly those of localization — where does the phenomenon start ? In recent years, more dynamic questions are being asked — what is happening ? How does it come about ? What are the mechanisms ?

If we think of the problems of the nervous system as the physiologist and neuroanatomist are doing more and more today, as problems of *how*, rather than of *where* things happen, recognizing fully that the where is a necessary but not a sufficient condition of understanding then that most dramatic manifestation of neural action the tremendous over-activity seen in convulsive discharges, should serve to focus the organizational, the chemical, the electrical and the physiological approaches to neural problems The present and future hopes for handling convulsions are similarly the hopes for understanding neural action

This symposium was planned for today along such lines of thought, not by myself alone as Dr Jasper indicated last night but by several others one of the most useful being Jasper himself The speakers have not had a chance to talk to each other Some have not been able to give discussants manuscripts and each is perhaps not entirely sure of his role in the total picture, but I have such confidence in the men as individuals as to anticipate a thoroughly coordinated program If there is time at the close of the formal presentation and I very much hope there will be, we will solicit free discussion from the floor Dr Wilder Penfield, as speaker, and Dr Herbert Jasper as discussant, both of Montreal will open the symposium by considering "The Functional and Electrical Responses of the Brain to Epileptic Discharge"

EPILEPTIC MANIFESTATIONS OF CORTICAL AND SUPRACORTICAL DISCHARGE[1]

Wilder PENFIELD, M D , F R S
Montreal Neurological Institute

The validity of the Jacksonian conception of an ictal ganglionic discharge has been verified by the clinical use of the electroencephalograph But the disturbance of electrical rhythms of the brain during a seizure is only one of the manifestations of an attack It does not tell the whole story of epilepsy The clinical picture is also important and we must enquire into the pathological cause

In opening a symposium of this type attention may well be directed to the conception that in clinical epilepsy seizures begin with ganglionic discharge in some specific location within the brain and this applies to all types of case Since the nature of cause and the site of origin of discharge vary a plan of classification will be outlined before consideration of the nature of cortical responses to epileptic discharges

The attempt to classify cases of epilepsy on electroencephalographic evidence alone under such headings as petit mal grand mal and psychomotor was useful but it had certain drawbacks It tended to stop the study of a case before it was completed From a practical clinical point of view, only the petit mal subdivision is useful

A CLASSIFICATION

Thanks to the pioneer work of Gibbs Davis and Lennox (1935) an expert is now able to recognize a three per second rhythm as characteristic of idiopathic (essential genetic) epilepsy Bursts of such rhythms accompany the minor lapses of consciousness which have been called petit mal But such lapses may develop into major generalized convulsions With this generalization the electrogram changes from bilaterally synchronous three per second waves into a bilateral discharge of rapid spikes You may call this grand mal if you like but the electrographic picture does not differ from that recorded during a generalized convulsion in symptomatic epilepsy

Consequently grand mal both clinically and electrographically is not a subdivision of the epilepsies It describes the end result of a seizure which may have begun with bilateral three per second rhythms with bilateral six per second rhythms, or with spike discharges localized to one of the various areas of the cerebral cortex

It would be quite free of confusion to subdivide cases of idiopathic epilepsy (or if preferred genetic cryptogenic or essential epilepsy) into those in which only petit mal attacks appear or only grand mal or both petit mal and grand mal seizures In other forms of epilepsy the small attacks may be called minor and the larger attacks major seizures

The disturbance of electrical rhythm is maximum in the midfrontal region and appears simultaneously as a reversed (mirror) image in the midfrontal region of the other side There is good evidence to believe that the origin of these widespread discharges is to be found in diencephalon and mesencephalon[1] (Morison and Dempsey 1942 Penfield and Jasper 1947 Jasper and Fortuyn 1947) This is the distinguishing characteristic of idiopathic epilepsy

The epileptic attack may be considered a symptom of the discharge that is occurring in the gray matter or it may be looked upon as a symptom of the pathological condition

[1] From the Department of Neurology and Neurosurgery McGill University and the Montreal Neurological Institute Reprint no 284

[1] These areas of gray matter are commonly referred to as subcortical in position But from a functional point of view they are *supracortical* They represent a level higher in the scale of functional representation than the cortex This explains the reference in the title of this paper to cortical and supracortical discharge

which is the cause of that discharge But classification of the epilepsies should serve the clinician as guide to therapy and to prognosis To that end we should seek in a classification to indicate first the site of initial epileptic discharge and secondly its cause

The search for cause compels the clinician to go farther Idiopathic epilepsy would seem to be due to an abnormality of cerebral physiology which has, at least, as much of a genetic background as migraine Focal cerebral seizures are produced by abnormality within some area of gray matter, usually the cortex The abnormality is a continuing state affecting the ganglion cells It seems to be associated with local decrease in the amount of oxygen that reaches some portion of the area in question The cause of this change may be compression due to an expanding lesion such as tumor or abscess It may be laceration of cortex due to trauma and followed by contracting scar It may be the shrivelled gyrus that was partially destroyed by natal ischemia or by cerebral vascular accident

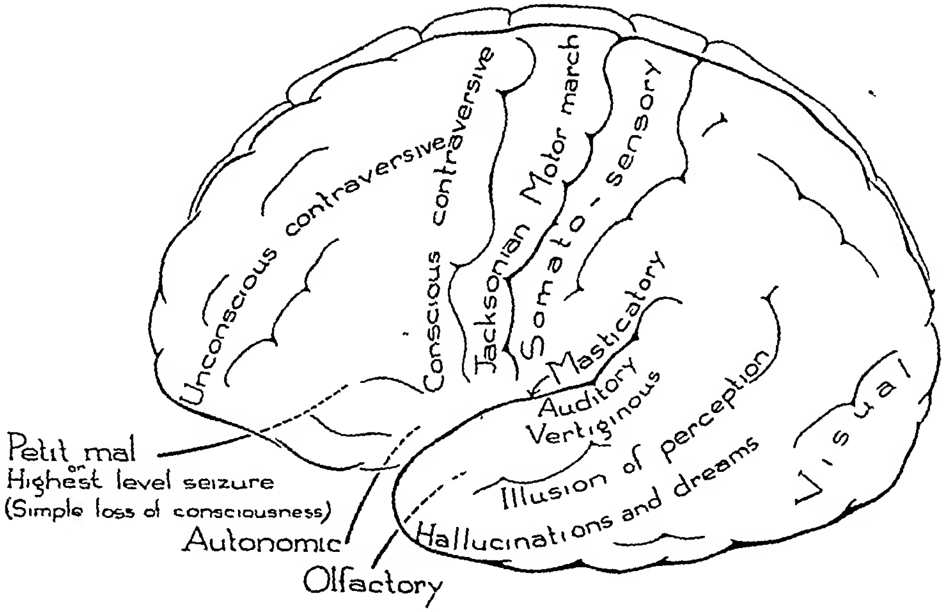


Fig 1 Patterns of seizure onset in relation to the site of origin of the epileptic discharge which produces each (Penfield 1948)

No useful purpose is to be served by dropping the term epilepsy but it may well be reserved for patients who suffer from idiopathic epilepsy Until the type of seizure is identified, we find it useful to employ the term cerebral seizures (Table I) Study of seizure pattern and of electroencephalogram will then make it possible to withdraw from this group the cases identified as idiopathic epilepsy and the cases of focal cerebral seizures

Table I
CLASSIFICATION

I Cerebral Seizures
  Cause
II Focal Cerebral Seizures
  Localization
  Pattern
  Cause
III Idiopathic Epilepsy

In the search for the exact location of the initiating discharge one must examine the pattern of the beginning of the seizure or of the minor attack whether this is sensory motor or psychical This provides us with the first clue to the localization of the focal discharge The situation of an electrographic spike' focus on the surface of the scalp also has great localizing value, if we

allow for the possibility of error in the projection from cortex to scalp an error that will not usually be greater than 2 or 3 cm if the focus lies on the convexity of the hemisphere

A case which has been identified as one of focal cerebral seizures may be further classified as to cause location and pattern of attack (Table I) Thus a patient with Jacksonian motor seizures might receive the following diagnosis — *Focal Cerebral Seizures* localization — *right precentral* pattern — *somatosensory* cause — *birth injury* Reference to figure I summarizes a few of the other common seizure patterns in relation to their cortical localization Thus another patient who complained of a strange sense of familiarity (deja vu phenomenon) followed by automatism might be classified as *Focal Cerebral Seizures* localization — *right temporal* pattern — *psychical illusion* and *automatism* cause — *brain tumor* Another who became unconscious and was then observed to turn around to the right before falling in a generalized seizure might be classified as follows *Focal Cerebral Seizures* localization — *left anterior frontal* type — *unconscious adversive* cause — *unknown*

The initial EEG interpretation may give clear evidence of genetic epilepsy or it may discover a circumscribed spike focus but often conclusion must be postponed for later study It will be necessary to leave some patients in the classification of cerebral seizures (Table I) cause unknown or cerebral seizures cause — hypoglycemia and so on

It is obvious that the work of sorting out the patients who complain of seizures calls for combined clinical and electroencephalographic study and such study has already led to new and exciting advance in our knowledge of human neurophysiology

B CORTICAL RESPONSES

The response elicited from the cerebral cortex as the result of spontaneous local epileptic discharge can be initiated in most areas of the brain by electrical stimulation There is one major exception to this statement Curiously enough stimulation of the anterior frontal region rarely produces a seizure although spontaneous seizures begin there as they do elsewhere.

There is a great variety of response when different areas of cortex are activated as shown by the partial outline in table II The movement produced from the Rolandic convolutions and the sensation from there and from the other sensory areas are positive phenomena but they are very elementary in character no skilled action and no complete picture no words no music Discharge in the elaboration areas such as those for speech produces only arrest of skilled movement It produces aphasia not speaking

TABLE II

Some Results of

CORTICAL ACTIVATION

1 MOVEMENT — Somatic
2 SENSATION — Somatic Visual Auditory Olfactory Vestibular
3 ELABORATION ARREST — Speech and other Skills
4 PSYCHICAL HALLUCINATIONS AND ILLUSIONS
5 CONFUSION OF THOUGHT AND UNCONSCIOUSNESS
6 MISCELLANEOUS — Looking Forced thinking Autonomic Phenomena etc

In the temporal cortex the response is both positive and elaborate Here well-formed hallucinations of sight and sound are occasionally produced — memories dreams and perceptual illusions

In the anterior frontal region the result of discharge is again negative An attack arising here may produce initial confusion in thinking that is detectable by an observer but of which the patient is not aware The confusion is followed by turning and loss of consciousness

Local Fits

Electrical and epileptic stimulation may or may not have a positive effect but it invariably has some negative effect although it may not always be easy to demonstrate its

nature The negative effect is explained by the fact that the area stimulated is paralyzed for its normal uses during the ictal discharge and during the immediately succeeding period of post-ictal exhaustion But it is often true that the effect of the stimulation can only be discovered if the patient is called upon to do something that depends on the function of that area during the paralysis

Some responses depend upon what may be called inborn neuronal patterns Others depend on acquired synaptic patterns It is obvious that motor phenomena which result from stimulation of the central cortex are inborn They are the same from individual to individual The order is invariable The extent of representation seems to be in proportion to the functional uses to which the parts are put by the adult But the responses to stimulation are the same in infancy and maturity

Stimulation of the motor cortex produces those movements of which the newborn human infant is capable, e g , simple extension and flexion of arm and leg with no delicacy of coordination but it also produces coordinated movements of vocalization of mastication sucking swallowing Similar skilled movements e g crying and feeding we bring with us into the world We are originally expert only in the arts of protest and self satisfaction The precentral gyrus is essential to the performance of the skilled movement acquired later in life and yet there is no change in the result of this form of artificial stimulation before and after the acquisition of skills

The same is true of the sensory areas of the cortex In the central cortex discharge produces only a sense of tingling or of movement in hand foot, tongue etc , in the occipital cortex gross lights shadows colors in the first temporal convolution the simplest of sounds, in the uncus distasteful odor The quality of odor perceived may have changed little during ontogenetic development but visual and auditory perceptions have become greatly elaborated Nevertheless the evidence of that elaboration is not found in the sensory areas of the cortex

In all these sensory and motor regions we find no evidence that epileptic discharge is capable of activating acquired neurone connections But in the cortex of the temporal lobe and extending back into parietal and occipital regions a little, there are synaptic patterns which must constitute the record of previous experience, the records of memory established in duplicate in comparable areas of the two sides

In this portion of the cortex spontaneous epileptic discharge may cause the patient to see or hear things which like his own memories exist for him but for no one else It is a psychical" experience (to borrow a word employed by Jackson) rather than a sensory one The elements of the hallucination are drawn from the patient's own memory records which are obviously laid down in that portion of the cortex The cortical record has lost its elementary character It corresponds with the perceptions of the individual and has added to it the individual's own reactions to the sight and the sound

Stimulation of the temporal cortex of a patient who has had no epileptic hallucinations does not produce one although he may say that it changes his thinking" or that he seems far away On the other hand when a certain hallucination has previously constituted the patient s minor seizure then stimulation may likewise produce that dream or a modification of it

Aside from the anatomical and physiological significance, these differences should throw light upon the nature of spread of the epileptic discharge Let us consider an active epileptogenic focus in the sensorimotor thumb area It gives evidence recorded in the electrogram of brief independent discharges between attacks and without producing clinical symptoms Periodically this inter-ictal fire gains sudden headway and the patient is aware of tingling in his thumb He is having a minor seizure comparable to the petit mal of the idiopathic epileptic The characters of these two minor seizures differ greatly because of the difference in the function of the gray matter where the fire is burning

Let us suppose that the discharge that is going on in the thumb area is sufficiently intense to cause it to spread A Jacksonian march is then set up into contiguous cortex and the patient may begin to feel a tingling in his face in addition to that in his thumb The pattern of that cortical spread is not determined by any particularly close functional relationship that exists between the thumb and that side of the face It is determined merely by the fact that anatomically the sensory representations of face and thumb lie next to each other

Now let us compare with this the probable mechanism of a psychical hallucination As discharge in a temporal focus flares up it seems to set off activity in certain ganglion cells which are scattered over the temporal region but which are bound together in a synaptic pattern

The activity thus artificially produced in this pattern causes the patient to be aware of an experience which he is apt to say is like a dream He hears and sees people carrying out action The elements of the hallucination are derived from his own memory for his mother or his friends may be there in familiar surroundings yet he recognizes that this is different from a memory that he would himself summon It is obvious that the discharge of the epileptogenic focus has activated an acquired neurone pattern, not an inborn one

In such a case the stimulating electrode may also activate the same hallucination when the cortex is exposed Action goes forward as in a dream until the electrode is withdrawn when the hallucination may vanish without evidence of after discharge Likewise if the electrode is applied to the proper point on the postcentral gyrus a sensation may be produced in the thumb It continues while the electrode remains in place and stops on its withdrawal

In the one case a sensory phenomenon is being produced in the other a psychical phenomenon The pattern in the temporal cortex is selected by the excitation only because previous facilitation has made it dominant It is only one of a great many possible neurone patterns in which are filed away the experiences of an individual But the whole ganglionic mantle is not involved in epileptic discharge during the hallucination It is the nature of memory that movement may go forward in it This does not mean epileptic spread but may apparently be produced by stimulation that remains local

However if the epileptic discharge that is localized to one area of temporal cortex during the production of a hallucination should begin to spread it would do so into contiguous areas of cortex Then it seems likely that the hallucination would come to an end It would be crowded out as other phenomena make their appearance

Discharge within the temporal cortex may also produce illusions The things that the patient is looking at the sounds that he hears the position of himself in regard to his environment may seem to him to be strangely altered These are illusions of perception He feels that he has experienced it all before (deja vu phenomenon) or that it is absurd or things are far away or suddenly near or he himself seems to be far away in space and to be observing himself He is not unconscious of course and he maintains an awareness of the reality of things as well as of this distortion of his own perceptions He is even then using his memory records for he makes a judgement by comparing the present perception with what his memory tells him he should expect

Hughlings Jackson with whimsical insight called this state of double consciousness — mental diplopia Even during a hallucination the subject is usually dimly aware that he is dreaming

It is obvious therefore that the temporal cortex and some adjacent cortex serve the uses of memory recording for the hallucinations are made up of remembered experience and inasmuch as the patient later remembers the details of the hallucination it is possible that he employs the other temporal cortex for the purpose But if the attacks that involve the temporal region (and also those

of the island of Reil) spread further the subject is apt to become amnesic He may even have a retrograde amnesia that expunges the memory of his preceding hallucination or illusion

Such a patient might remember a smaller attack of, let us say, illusion after it was over But after a larger attack he would not recall the initial illusion although he may have indicated to an observer that he knew an attack was starting During the amnesia it seems likely that the central portion of the memory recording mechanism is disabled by spread of the discharging state along projection pathways Such amnesia is associated with automatism

C SPREAD OF EPILEPTIC DISCHARGE

There are two kinds of spread of the epileptic discharge

1 *Spread by contiguity* We have discussed this already In the cortex the altered state creeps along the gray carpet in one direction or in another producing clinical evidence of its advance electrographic evidence of increased potentials and marked increase in local blood flow It may thus pass from one cortical field into a functionally little related field

It is as though the initial focus were capable of forming a juice an 'Alpha substance'[1] which was capable of setting adjacent ganglion cells on fire and as though these new cells in firing poured out more substance and so the state is propagated across the surface until distant firing through projection tracts produces a generalized explosion

2 *Spread by projection* It is at once obvious that cortical areas are capable of transmitting this discharging state to areas of gray matter situated at a distance This is particularly true along the great projection pathways that connect the cortex with subcortical nuclei It would seem likely that axonal conduction of the enormous energy being released in the original focus might well overstimulate the second area through axonal pathways much as a stimulating electrode may do

D AUTOMATISM

The problem of epileptic automatism is of great importance In such a state the patient retains bodily control with little or no understanding of the meaning of things If it may be said that consciousness is present it is certainly in a much impoverished form and he will have no memory of what takes place during the automatism

The fact that there is such a thing as epileptic automatism suggests that there is within the nervous system an area of gray matter which is particularly related to the processes of understanding deciding and remembering It means, further, that this area of gray matter may be paralyzed without arresting an elaborate system of coordination between sensation and motor control

Some degree of automatism may follow any type of generalized convulsive seizure making its appearance during the period of recovery But without preliminary major attack it occurs chiefly in seizures which arise in the temporal region It also occurs as the result of petit mal discharge and less frequently, as the result of epileptic discharge in one anterior frontal region without major convulsion For the purposes of discussion we may refer to temporal automatism, petit mal automatism and frontal automatism

1 *Temporal automatism* Let us take as an example the patient who has just had the following psychical illusion He was suddenly seized with the feeling that what was happening to him had all happened before He remembered no more But those standing with the patient might have seen him swallow and perhaps salivate actively They observed that their companion had changed He was not the individual they knew but, by startling metamorphosis, a complete automaton capable of vigorous resistance but not open to reason, devoid of understanding

The explanation of this change is that at the time of the onset of automatism the

[1] See PENFIELD 1937

ganglionic discharge in the temporal cortex had presumably extended its influence from the cortex along projection pathways into the gray matter in the diencephalon and midbrain, thus inactivating this gray matter It is at this higher level that the neural mechanism is located which is essential to the process of memory-recording in both temporal fields It might seem that he was for the time being cut off completely from the body of his past experience but he was otherwise capable As the discharge spread by projection to this higher level it may have been spreading also by contiguity into Sylvian or insular cortex thus causing him to swallow and to salivate But he remembered no more than the illusion

2 *Petit mal automatism* It is not always easy to differentiate between petit mal automatism and temporal automatism In petit mal there is no warning no lesser attack that precedes the state and usually no mastication or salivation only a stare' which warns the patient s friends that something has snuffed out conscious perception although he may not fall The petit mal is usually of much shorter duration than temporal automatism The temporal automaton is apt to wander off to a distance and to fight when attempts are made to control him This would be rare indeed during petit mal attacks

3 *Frontal automatism* States of altered consciousness with confusion and stereotyped thinking or behavior may also be produced by epileptic discharges arising in anterior mesial or orbital portions of one frontal lobe In some cases automatic behavior may result which also simulates closely that caused by discharges of temporal origin In such cases the accompanying electrographic disturbance may resemble the slow petit mal rhythm but is not identical with it This will be elaborated in the contribution of Dr Jasper to this symposium

In all cases of automatism the epileptic discharge may be said to have affected the [illegible] matter that constitutes a higher level of integration than the cerebral cortex Discharge evidently produces local paralysis of function at that level as it does elsewhere This highest level the 'seat of consciousness" is not a point Neither is it an isolated nucleus It is made up of parts which seem at times to be differentially inactivated

However the conclusion with regard to the highest level' which may be drawn from the above reasoning is that it includes gray matter and that it may be inactivated by epileptic paralysis without paralyzing the sensorimotor integrating mechanism In the integrating mechanism that is still active during automatism there is an effector mechanism and a mechanism for the reception of the afferent streams of information but there is no memory-recording system If the effector or motor mechanism is involved in discharge the patient has a generalized seizure also without subsequent memory But he is then obviously incapable of automatic behavior except during a brief phase of the recovery from his attack

From the electrographic point of view it would seem that in petit mal the discharge which produces automatism originates in that portion of the highest level complex which activates the three per second rhythm On the other hand in temporal automatism there is involvement of the neuronal circuits which are responsible for the six per second psychomotor rhythm

In each case the patient shows the negative or inactivating effect of an epileptic discharge that is occurring in a central mechanism As in all seizures the negative or paralytic effect appears during discharge and during the immediately succeeding period of ganglionic exhaustion Automatism therefore is an ictal phenomenon and a post-ictal phenomenon as well

The temporal automaton has been cut off completely from the body of his previous experience through a mechanism related to the psychomotor rhythm His condition is not psychomotor however but *psychoparetic* Actually in all automatism there is paresis of a portion of the highest level of neural integration and therefore all automatism may be said to be psychoparetic

REFERENCES

Gibbs F A, Davis H and Lennox, W G Electro-encephalogram in epilepsy and in conditions of impaired consciousness *Arch Neurol Psychiat*, Chicago **1935** *34* 1133-1148

Jasper H H and Droogleever-Fortuyn J Experimental studies on the functional anatomy of petit mal epilepsy *Res Publ Ass nerv ment Dis* **1947** *26* 272-298

Morison R S, and Dempsey E W A study of thalamo-cortical relations *Amer J Physiol* **1942** *135* 281-292

Penfield W and Jasper H Highest level seizures *Res Publ Ass nerv ment Dis* **1947** *26* 252-271

Penfield W The circulation of the epileptic brain *Res Publ Ass nerv ment Dis* **1937** *18* 605-637

Penfield W The surgical treatment of focal epilepsy British Surgical Practice London Butterworth, **1948**

ELECTRICAL SIGNS OF EPILEPTIC DISCHARGE[1]

Herbert H Jasper, M D , D es Sc

Montreal Neurological Institute

FOCAL CORTICAL DISCHARGE

There is only one form of electrical activity which we consider pathognomonic of a *local* primary discharging lesion which may be epileptogenic This is the random spike discharge It is a rapid surface negative wave of the order of ten to twenty milliseconds duration when recorded at its source on the cortex When recorded directly at its source on the exposed brain, it may reach 500 to as high as 2000 microvolts in amplitude When obtained through the skull and scalp these spikes are attenuated in amplitude and prolonged in time They appear on the scalp as aperiodic rapid waves of about twenty to forty milliseconds duration and with voltages from about 50 to 500 microvolts

Random spikes are similar in form regardless of the cortical area from which they are obtained They do not seem to depend upon the cyto-architectural structure of any given area of cortex but seem to be a surface discharge probably of only the superficial layers of the cortex when they are of small amplitude and relatively monophasic When they become increased in amplitude and contain a large diphasic component usually electropositive at the surface evidence of conduction to a distant area may be found The conducted wave recorded at a distance is temporally dispersed appearing as a sharp wave that is a wave of rapid rising phase but prolonged falling phase These sharp waves may be of 50 to 200 milliseconds in duration and they also are of the same form regardless of the area of cortex from which they are recorded In figure 1 is shown a local spike discharge together with multiple spikes from an area of *cortex just above the Fissure of Sylvius* Conducted waves just below the Fissure of Sylvius show the temporal dispersion which occurs with this type of conduction across a fissure in one hemisphere

To those who are familiar with the strychnine spikes which have been used to such advantage by Dusser de Barenne and McCulloch (1939) and their associates it will be *seen that the spikes of the epileptogenic,* lesion in man are comparable in almost every respect It is surprising that their conduction along fibre tracts does not interfere to a greater extent with localization studies of the focus of spike discharge although mirror foci are occasionally seen When the spike is of superficial origin on the convexity of the cortex just beneath the skull and when it is of moderate amplitude little evidence of conduction is apparent either from the homologous area of the opposite hemisphere or from other areas of the same side If, however this local spike process is buried in a fissure such as within the island of Reil or if its origin is within the *longitudinal fissure or on the undersurface* of the brain it cannot be ordinarily recorded from the scalp surface What is recorded then are only the conducted disturbances where they may appear as prolonged sharp waves or as rhythmic potential waves They may be predominantly from one hemisphere or perhaps bilaterally from both hemispheres as the spike process activates mechanisms firing to both sides of the brain

These hidden spike foci may be very difficult of discovery in the usual E E G examination They may be so precisely localized that they are missed in the routine E E G with a limited number of electrodes on the scalp surface or they may arise in *a buried atrophic gyrus and no evidence of* their presence may be seen from the scalp

[1] From the Department of Neurology and Neurosurgery McGill University and the Montreal Neurological Institute Reprint no 287

surface In many instances we have found them only when electrodes were placed directly over the buried gyrus on the exposed cortex, or on the mesial or ventral surface of the hemisphere

The random spike when appearing at relatively infrequent intervals and of only moderate voltage, is scarcely ever associated with any apparent change in the patient either objectively or subjectively Changes in the patient are seen only when they begin to fire repetitively and attain a higher voltage This seems to be consistent with the necessity for summation in the activation of the cortex, since single shocks producing single responses from the cortex are also unable to produce outward signs of excitation (Adrian 1936 and Adrian and Moruzzi 1939)

irregular sequence that the convulsive movements of the left hand began At first this rapid firing of local spikes is disorganized but it soon becomes integrated into a regular rhythmic discharge Not until this regular rhythmic discharge develops and the process begins to spread to other areas or perhaps more probably to subcortical structures, is there an effect on consciousness

Another characteristic of a focal epileptogenic lesion is the facility with which after-discharge may be induced in it, following electrical stimulation This method of locating areas of cortex which seem susceptible to epileptic activity has been developed by Walker (1947) and we have recently had the opportunity of confirming this observation in a number of patients It was our first impression that the area from which

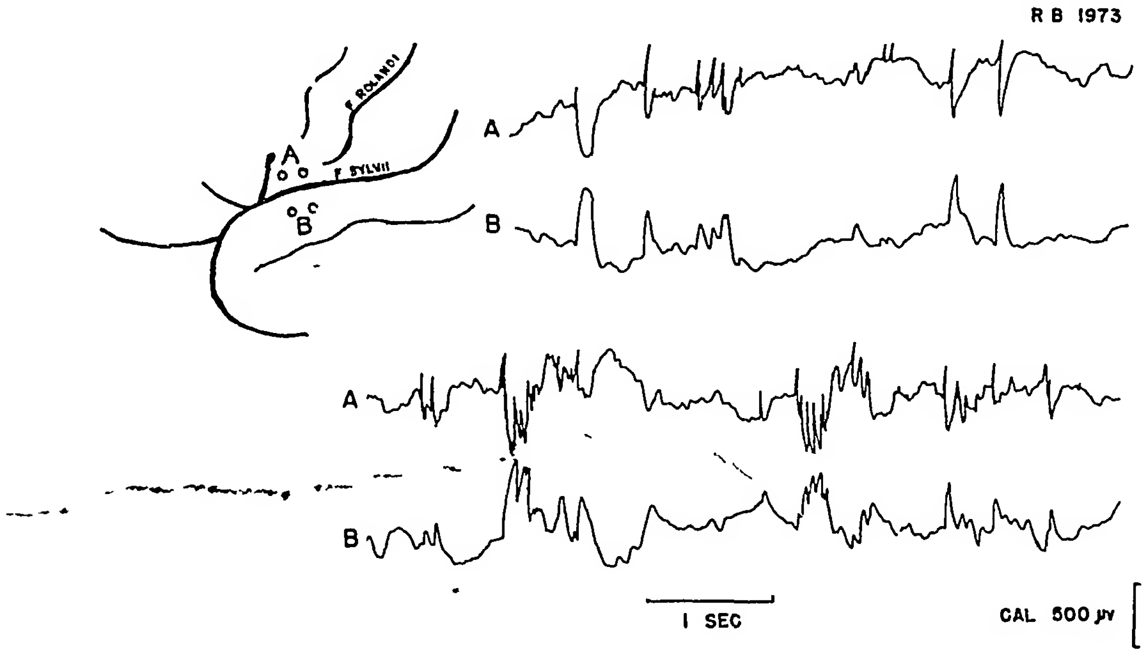


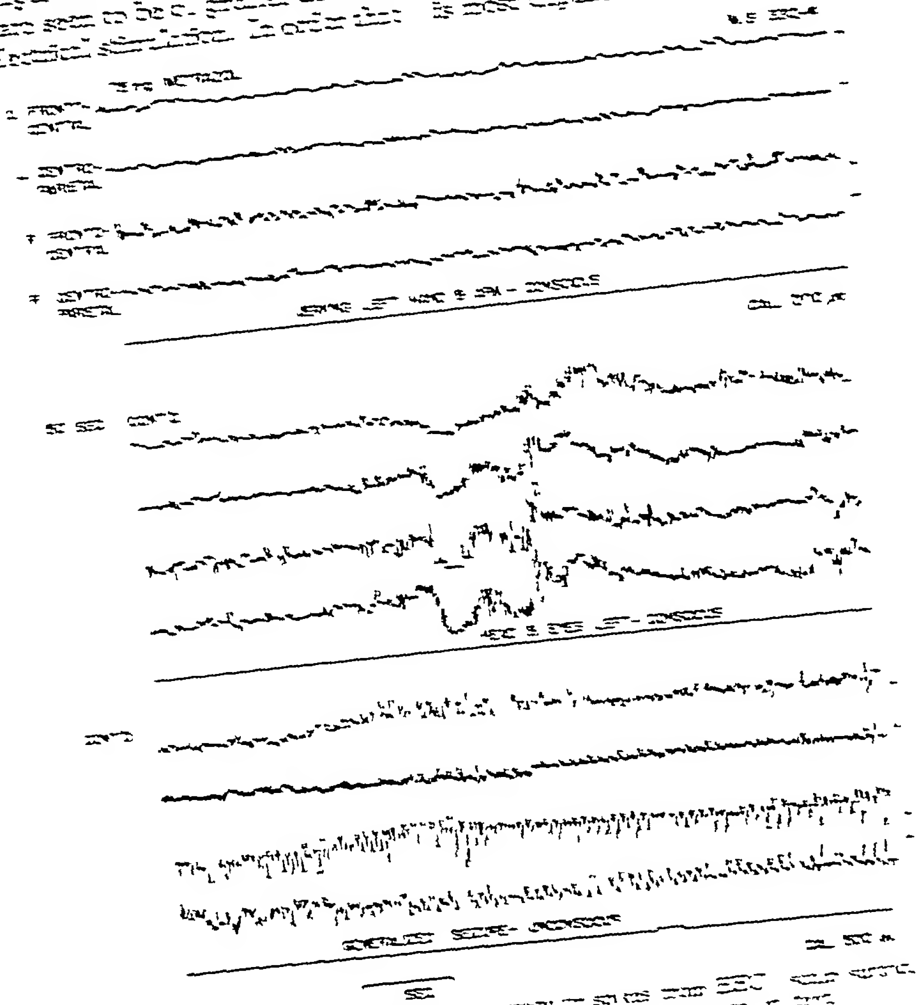
Fig 1 Random spike discharges appearing spontaneously in the electrocorticogram of a patient with focal seizures arising on the border of an epidermoid tumor The spikes arising from just above the Fissure of Sylvius at A are initially surface negative with a longer positive phase when conducted out of this local area to B across the Fissure Note temporally dispersed conducted waves in lines marked B

The development of a random spike focus into a clinical seizure is perhaps best illustrated in an example from a patient with Jacksonian epilepsy with a spike focus in the right precentral hand area As shown in figure 2 it was not until the spikes began to repeat themselves in a fairly rapid but still

random spikes were obtained spontaneously did not always correspond to the area from which after-discharge could be most readily induced following electrical stimulation However, with further study we are inclined to agree with Walker in that with most patients the area from which random spikes

ELECTRICAL SIGNS OF EPILEPTIC DISCHARGE

are obtained is also the case from which after-discharges may be most readily in[illegible] and are seen to be of greater duration following electrical stimulation. In order that [illegible] with protocol may be used when paroxysm[illegible] But the spontaneous discharge usually pre[illegible] sent without the help of these artificial agents is most dependable.



[illegible]

this method may be used however [illegible] care must be taken in [illegible] the [illegible] of the strength and duration of [illegible] [illegible] [illegible] [illegible]

SPREADING EPILEPTIC ACTIVATION OF THE CORTEX

[illegible]

zures but may accentuate petit mal Hence the slogan, Fit the Treatment to the Fit"

A third conception inherited from the days of sedation is that an effective antiseizure remedy is only a symptomatic stop gap — a barrier that holds seizures in check, but effects no cure This conclusion is generally accepted, but rests I believe on general impressions rather than on controlled statistical studies We all know that if medication is abruptly discontinued within a few days the patient is likely to have a recurrence of seizures with not just a return to the former frequency but an unusual number or n unusual severity of attacks This general servation needs to be studied in detail Whether the stopping of medication is attended by an outpouring of attacks may depend on the type or frequency of seizures on the medicine used and on the duration of medication Though all these points deserve study probably the last named is the most fluential If seizure control has been brief, the number of seizures that follow removal of the medicine may equal the number that did not appear during the period of control If however, control has been maintained for a long period, possibly years, only a fraction of the retained seizures or possibly none will appear when medicine is discontinued

For example a patient of ours having approximately 150 petit mal a day was kept seizures free for four to five days by the use of phenobarbital or by short periods of acidosis In the several days that followed these treatments approximately all the retained seizures appeared (2) In contrast, maintenance of ketosis for 33 days resulted in approximately 5 000 petit mal saved (3) At a later time when seizures numbered only 40 a day, eight months of ketogenic diet halved their frequency (4) Termination of ketosis did not result in even temporary increase of petit mal so that another 5 000 seizures were saved Presumably the mechanisms of chemical control by ketosis and by medicines run parallel but different drugs and types of seizures may yield different quantitative results For example a number of our patients have had no return of their multitudinous petit mal when tridione was stopped, even though seizures had been absent only a few months

In the examples cited, the analogy of an anticonvulsant as the dam of a reservoir does not hold unless we postulate that channels for the entrance of water are blocked also How else explain the indefinite absence of seizures after cessation of medication In conclusion then successful drug therapy may mean correction of a disorder, and not merely its suppression

Various questions await answer Is the length of time required for a drug to take effect simply a matter of accumulation of an adequate concentration of tissues, or is it a gradual improvement of cellular metabolism or of the transmission of impulses, or of whatever causes seizures ? Yet another difficulty awaiting explanation is the ability of a given drug to control seizures in one patient and not in another, or in a given patient at one time and not at another

Such problems could be better explored if there were means of measuring drugs in body fluids Of the anticonvulsants now in use, only bromide can be measured readily Measurements of bromide demonstrate that its effectiveness is not simply a function of its concentration in the blood

SEIZURES AND DYSRHYTHMIA

Electroencephalography offers a means of answering some of the problems just propounded Berger demonstrated disorders of rhythm during epileptic seizures Such demonstration would have had limited clinical use, but for the finding of paroxysmal discharges in the records of patients when they were free of seizures We spoke of these as larval" or subclinical seizures and called epilepsy 'a paroxysmal cerebral dysrhythmia' (5) The Gibbs have determined the incidence of various types of interseizure electroencephalograms in epileptic patients as compared with non-epileptics (6) A study of these data demonstrates the extreme variety of dysrhythmias and the great differences in their diagnostic significance

However, experience has shown that normal persons may have gross abnormalities of rhythm without ever having had epilepsy Therefore paroxysmal dysrhythmias may be either symptomatic or asymptomatic The difference between these two may be almost nil as in the following example

A and B are monozygotic twin girls aged nine Except for eclampsia and possible migraine of the mother there is no significant family or past history A year ago the school teacher told the mother that A was having transient lapses of consciousness The electroencephalogram disclosed a typical dart and dome discharge accompanying clinical petit mal and also frequent short subclinical' discharges Twin sister B though devoid of petit mal had even more subclinical discharges than A and during overventilation there was a prolonged burst of spike and wave complexes during which she was unconscious In this child the distinction between dart and dome dysrhythmia and petit mal epilepsy is so paper thin that a few deep breaths blows it away and makes her really and not just potentially epileptic

Correlation of bodily and of cortical disorders are most easily made in persons subject to petit mal seizures A solitary spike and wave may or may not be attended by a single sharp contraction of muscles (a myoclonic jerk) or by a sudden loss of muscle support (an akinetic seizure). A series of spike and wave formations several seconds in duration will be symptomless but if longer will be attended by unconsciousness and possibly by small rhythmic movements (petit mal) Rarely these longer sequences are symptomless Uniformly the long sequences of high voltage three per second waves (similar to those of petit mal except for the absence of spikes) that may follow hyperventilation are symptomless

How is symptomatic as opposed to asymptomatic dyshrythmia to be explained? Why are the clinical manifestations of a stereotyped pattern so different? What does a dart and dome have that a dome doesn t have? Why is a big smooth wave more related to petit mal than one with a crenated contour? Why are the three and the two per second spike and wave formation so different in clinical manifestations and in response to medication? Explanations are even more difficult when tracings show no paroxysmal high voltage discharges but only alteration of the dominant frequency Usually, therefore something more than disordered brain rhythms are necessary for a fit A missing ingredient might be called facilitation or more safely an externalizing mechanism The nature of this is a fascinating study for future investigators

DYSRHYTHMIA AND PHARMACOLOGY

Although the human electroencephalogram is a constitutional characteristic — an hereditary trait it is a fluid trait The earliest clinical observations in this country demonstrated the wave changes induced by altering the oxygen and the carbon dioxide content of the blood (7) or by the administration of drugs (8) Numerous observations have been made since The action of sedatives commonly used in epilepsy on the electroencephalograms of normal subjects has been reviewed by Margaret Lennox (9) The background rhythm may be quickened or (less often) slowed depending on the individual or the dose The electroenphalographer must consider this complicating effect when interpreting the records of patients taking antiseizure drugs However these faster waves are of low voltage The more significant bursts of high voltage waves may occur during drug induced sleep but doubtless sleep rather than the medicine is responsible

Low voltage fast or slow frequencies are of much less interest to us than paroxysms of high voltage fast or slow waves aptly called seizure discharges We early found that intravenous injection of a convulsive drug brings on seizure discharges in the time required for the blood to travel from the arm to the brain Conversely injection of anticonvulsants wipes them from the record (10) More clinical interest attaches to the influence on abnormal electroencephalograms

of medication given in therapeutic amounts by mouth over extended periods of time

Case reports from a number of authors attest the partial or complete disappearance of gross abnormalities of rhythm of certain patients receiving drug therapy However, results with one or a few cases do not permit generalization nor definition of the influence of the various factors involved, such as age of the patient, type and cause of dysrhythmia and the medicine used Also of great practical interest is the relative effect of medicine on seizures and on seizure discharges

PHARMACOLOGY, SEIZURES AND DYSRHYTHMIA

If as all workers agree, gross irregularities of frequency and voltage of waves is a basis or concomitant of epilepsy, the assumption that dysrhythmia will automatically disappear along with seizures is an easy one Yet every electroencephalographer knows better Dysrhythmia may not appear in the routine record of an epileptic for the following reasons abnormalities occur too infrequently to be caught in a 20 minute recording, they are erupting in some portion of the brain other than the cortex, or adequate stimulus (overventilation, sleep, metrazol) was not employed

Granted that abnormalities were observed before treatment began, and the same electroencephalographic technique was used throughout if seizures and dysrhythmias follow opposite courses, one increasing while the other decreases doubt is cast on the value of successive electroencephalographic examinations in judging progress and prognosis However an adequate period of observation must be allowed because increasing dysrhythmia in the face of freedom from seizures may prophesy a return of seizures

However, problems of neurological mechanism are involved If medication stops both dysrhythmia and seizures it must correct or prevent the original abnormality If medication stops seizures but not interseizure dysrhythmia it may act by preventing the ever present minor discharges from becoming the excessive and prolonged outburst that coincides with the fit If under treatment the electroencephalogram becomes normal, but seizures continue there would seem to be little relation between the cortical dysrhythmia and convulsions

The only statistical significant observations so far recorded seem to be those of Hoefer (11) He examined the successive records of 96 patients Although in adequately treated cases the electroencephalogram becomes more normal", in a group of 40 patients whose seizures had disappeared under treatment 31 or 79 percent had paroxysmal activity for six months or more after seizures had ceased In about one half of these the abnormal activity was observed only after overventilation Data are broken down with respect to the type of clinical seizures but not the type of brain wave pattern No account was taken of electroencephalograms that were improved nor of course of paroxysmal activity that might have existed before epilepsy began when the person was normal'

CORRELATION OF CLINICAL AND EEG RESULTS

Dr Chaskiel Grossman examined the records of 100 of our private patients These patients were of all ages Those with definite evidence of brain damage were excluded Patients with clinical and electroencephalographic evidence of one or more of the petit mal triad were given tridione or paradione Those with grand mal or psychomotor seizures were given phenobarbital dilantin or mesantoin Because both clinical and electroencephalographic results are subject to day to day variations and because improvement in one may lag behind the other, we attempted merely to ascertain whether the clinical and electroencephalographic observations followed a broadly parallel course Each case was classified as to whether under treatment the seizures were absent were fewer or were unimproved and whether the dysrhythmia was absent, improved or unimproved Thus as shown in the accompanying tables each case fell in one of nine categories Patients whose initial electroencephalograms were normal were excluded for these could

not be improved Judgment of clinical improvement was based on the frequency of attacks before treatment was instituted The periods of treatment and the intervals of time between electroencephalographic examinations were variable If patients had petit mal, the time intervals were shorter than for other patients Of the 100 patients, 108 correlations were made, the duplicates representing different stages of treatment or differing dysrhythmias in certain patients

Because the members of the petit mal triad and the three per second dart and dome dysrhythmia are so clearly related patients having both were placed in a separate group If other types of seizures and of dysrhythmia were present also the patient was considered as being two cases Cases presenting slow spike and wave discharges (petit mal variant) were excluded because of their association with brain pathology

The data for the 59 cases of petit mal are expressed in table I The overall comparison, expressed as percentages of the 59 cases is as follows

	Seizures	*EEG*
Normal	37	29
Improved	40	32
Unimproved	23	39

instance was the record worse In contrast of the 13 patients whose petit mal did not improve under treatment none had an improved electroencephalogram

Expressing the results with reference to electroencephalographic changes of the 17 patients whose electroencephalograms became free of spike and wave formations 16 were free of petit mal whereas of 23 cases without electroencephalographic improvement only one was seizure free

Evaluation of data is more difficult and more open to error in patients having grand mal or psychomotor seizures because the intervals between seizures are wide and variable, and electroencephalographic abnormalities are variable and not distinctive They include greatly increased or decreased frequency of the dominant rhythm (F_2 and S_2 in the Gibbs' Classification) high voltage fast or slow paroxysmal discharges (except spike and wave) or spikes and an abnormal build-up" with overventilation Low voltage 15 to 20 per second activity was disregarded because this might be due to the medication Decision regarding improvement was based on whether the record as a whole was better at the end of a period of treatment than at the beginning Tabulation was

Table I — The clinical and EEG results in patients treated for petit mal

Clinical Results			*EEG Results — Spike and Wave*						
			Normal		*Improved*		*Not Improved*		*Total*
Seizures	No	%	No	%	No	%	No	%	%
Absent	22	37	16	72	5	23	1	5	100
Fewer	24	40	1	4	14	58	9	38	100
Unimproved	13	23	0	0	0	0	13	100	100
Total	59	100	17	29	19	32	23	39	100

Obviously electrical improvement lags behind clinical improvement These data do not indicate how far behind in point of time Of 22 patients made seizure free the records of 72 percent contained no spike and wave discharges and the records of only five percent were not altered for the better In no

from reports and not from original tracings but these tracings had been interpreted by one person

Results are displayed in table II As shown in the second column and the bottom line of the table 33 percent of the 49 cases were seizure free against only 14 percent

whose electroencephalograms were normal Conversely 30 percent were unimproved seizure wise and in 51 percent brain waves were no better

Table II — The clinical and EEG results in patients treated for seizures other than petit mal

Clinical Results			EEG Results — other than Spike and Wave						
			Normal		*Improved*		*Not Improved*		*Total*
Seizures	No	%	No	%	No	%	No	%	%
Absent	16	33	5	31	7	44	4	25	100
Fewer	18	37	2	11	9	50	7	39	100
Unimproved	15	30	0	0	1	7	14	93	100
Total	49	100	7	14	17	35	25	51	100

Although clinical improvement is not much below that experienced by petit mal patients, the electrical improvement was far less Of 16 cases seizure free, tracings became normal in only 31 percent, and were not improved in 25 percent Expressed with respect to the electroencephalograms of seven cases with normal electroencephalograms, five were seizure free whereas of 25 cases without electroencephalographic improvement, only four were seizure free

In order to compare cases of petit mal and other seizures more closely we ascertained the number in each group in which there was agreement in clinical and electroencephalographic results and the number in which one of these lagged behind Results were as follows

Clinical and EEG Results	*Petit Mal* No	%	*Others* No	%	*All* No	%
Changed categories together	43	73	28	57	71	66
Seizures improved more than EEG	15	25	18	37	31	30
EEG improved more than seizures	1	2	3	6	4	4

This tabulation indicates a general tendency for seizures and electroencephalograms to follow a parallel course In two-thirds of the cases if seizures were absent, improved or unimproved, the electroencephalograms were respectively, normal, improved or unimproved Correlation occurred more often in petit mal cases (73 percent), than in those with some other form of seizures (57 percent) In the 34 percent of all cases, in which strict correlation was not present, almost invariably the clinical improvement was greater than the electrical It was 12 times greater in petit mal cases and six times greater in others This study seems to indicate greater correlation than was reported by Hoefer This may be explained by the fact that our group of patients contained a much larger proportion of children with petit mal who were treated effectively with tridione Also, we took account of improved records, and not just those made normal

Petit mal cases are less subject to errors in tabulation That seizures should disappear more quickly than dysrhythmia supports the conception of dysrhythmia as structure and seizures as superstructure Medication affects the superstructure first, and only after an interval of weeks months or perhaps years, the underlying dysrhythmia Obviously the waves of the cortex are not the whole basis of seizures Usually, a convulsion is preceded not by tumultous waves but by a deadly calm, whereas the petit mal dart and dome appears on the record without wave warning In spite of the brilliant work of neurosurgeons and neurophysiologists the 'externalizing mechanisms that transform dysrhythmia into epilepsy need further study

SUMMARY

The interrelationships of pharmacology, seizures and dysrhythmia are discussed Cor-

relations have been made between clinical and electroencephalographic improvement in 100 patients receiving drug therapy The two follow a broadly parallel course changes in seizures and tracings being grouped simply as normal improved or unimproved In 66 percent of 108 periods of treatment there was complete correlation In 30 percent clinical improvement exceeded electrical improvement in four percent the reverse was true Clinical improvement and also complete correlation between seizures and dysrhythmia was more evident in patients with petit mal (73 percent correlation) than in those with other types of seizures (57 percent correlation)

Medication seems to influence seizures or an externalizing mechanism before it influences the dysrhythmia of an interseizure recording Broadly speaking repeated electroencephalograms assist in judging the progress of treatment and the prognosis of epilepsy

REFERENCES

1 MERRITT H H and PUTNAM T J Experimental Determination of Anticonvulsive Activity of Chemical Compounds *Epilepsia* 1945 *3* 51-73

2 LENNOX W G and WRIGHT L H Comparative Effects of Borotartrate and of Luminal on the Seizures of Epilepsy Boston M & S J 1926 *195* 1199-1207

3 LENNOX W G and COBB S Epilepsy from the Standpoint of Physiology and Treatment Williams & Wilkins Baltimore 1928

4 LENNOX W G Science and Seizures Harper and Bros 1946

5 GIBBS F A GIBBS E L and LENNOX W G Epilepsy A Paroxysmal Cerebral Dysrhythmia *Brain* 1937 *60* 377-388

6 GIBBS F A GIBBS E L and LENNOX W G Electroencephalographic Classification of Epileptic Patients and Control Subjects *Arch Neurol & Psychiat* 1943 *50* 111-128

7 GIBBS F A DAVIS H and LENNOX W G The Electroencephalograms in Epilepsy and in Impaired States of Consciousness *Arch Neurol & Psychiat* 1935 *34* 1133-1148

8 GIBBS F A GIBBS E L and LENNOX W G Effect on the Electroencephalogram of Certain Drugs which Influence Nervous Activity *Arch Int Med* 1937 *60* 154-156

9 LENNOX M Effects of Sedative Drugs on the Electroencephalogram *Am Jour Psychiat* 1946 *102* 799 804

10 LENNOX W G GIBBS F A and GIBBS E L Effect on the Electroencephalogram of Drugs and Conditions which Influence Seizures *Arch Neurol & Psychiat* 1936 *36* 1236-1245

11 HOEFER P HOFF H H and PLUVINAGE R I L The effect of Anticonvulsant Therapy on the Electroencephalogram of Patients with Idiopathic Epilepsy *Transactions Am Neurol Ass n* 1947 185

CLOSING STATEMENT

R W Gerard

Dr Jasper asked me to close this symposium by attempting to knit together the multiple threads that have been unwound before us In view of the richness of the material this is both an easy and pleasurable task

I am impressed first of all with the truly heartening progress that is being made in the study and conquest of epileptic phenomena What was a scant decade or two ago a disturbance known hardly better than in terms of its behavioral manifestations is today being resolved into meaningful categories each identified clinically electrically and chemically each subject to reasonably effective therapy and all at the verge of a true understanding of pathogenesis or at least of physiological pathology I cannot pass on without one other general comment

In this progress, indeed in this symposium is illustrated beautifully the almost standard course of advance The clinician surveying the phenomena nature offers, points out the problems demanding attention by simple observation or, better by powerful insight (Such a one is Penfield s clear demonstration that acquired neural patterns can be activated in temporal lobe focal seizures and that therefore no simple inborn derangement of fixed neural groups can encompass the entire problem Another is Jackson's mental diplopia) These problems then engage the attention of the experimenter who is rarely a clinician, at least primarily are fragmented and grappled with piece by piece in the laboratory and begin to yield partial answers The biological scientist then turns these findings back to the clinician for further exploration — witness the development of the modern antiepileptic drugs — and in time the doctor has at his disposal new and powerful therapies All this is normal and healthy and betokens the happy cooperation between explorer and analyst just as occurred between the field and laboratory biologists in the booming days of the past century What is not healthy about the present situation is the public relations aspect

Just as the creative effort of an individual mind starts with the conscious positing of a problem is followed by the really crucial unconscious work which reveals its answer and ends in a final conscious period of examination and checking, so the collective effort in solving clinical problems is in the public eye while the diseases remain flagrant challenges to the physician and reappears there when the doctor triumphantly applies the new remedies to his patients During the great labor of reaching the fruitful result the process fades from sight into the quiet laboratory The consequence is that people identify such progress with practicing physicians rather than with research biologists and public support when marshalled for new attacks becomes funnelled through clinical rather than laboratory channels

Biology is painfully weak on the national scene today in contrast for example to chemistry or physics and has been lost in the medical subdivision (except as intense effort has corrected this) in most of the great national scientific agencies It is to the advantage of the clinician no less than of the experimenter (to say nothing of the ultimate consumer — the citizen or patient) that the true situation should be made abundantly clear The unfolding story of our knowledge of epilepsy is a beautiful case in point

I turn now sharply to the content of this symposium The speakers have addressed themselves to three main problems they have been concerned with nosology and have offered evidence for the separate character as well as the separate locus of various kinds of epileptic manifestation they have given much attention to the spatial problems the pacemaker source of abnormal activity the mechanisms of activity spread within the

cortex or involving deeper white and gray structures the factor of re-excitation in this spread and finally the relation between the fire burning in the gray matter" and the smoke produced in the way of abnormal electrical motor, or psychic manifestations, and they have analysed and partly answered the problems of pathogenesis, of whether the discharging neurones are metabolically abnormal, are rendered excessively irritable by an altered chemical environment, are subjected to excessive excitation by neural barrage, or are deprived of their normal inhibitory restraint Incidentally, and not the least important, the study of this extreme condition of neural overactivity (or even of inactivity) is also illuminating the normal metabolism and function of the nervous system

Penfield and Jasper have emphasized the essential oneness of major discharges, whether arising from a cerebral focus by Jacksonian march or super-imposed upon petit mal episodes arising presumably in deep structures Yet Darrow, Toman and Lennox have re-emphasized the biochemical and pharmacological differences between the classical petit mal and grand mal seizures There is however no impossible conflict here As many of us have long emphasized, quantitative and qualitative metabolic differences between neurones and regions in the nervous system are the rule rather than the exception so that, and especially if different loci are involved, different chemical conditions might dispose to overactivity in different cases When activation exceeds a critical damping level, however, its further growth and spread would become independent of the particular and detailed situation which initially called it forth That the processes underlying seizures may indeed be in different categories is amply exemplified by the opposing action of CO_2 in grand and petit mal (high concentration favoring the former seizures low concentration the latter), by the different EEG patterns and loci by the greater effectiveness of tridione against metrazol convulsions and against petit mal and the greater effectiveness of dilantin against electrical convulsions and against grand mal We have, incidentally, suggestive evidence that the glutamic acid — glutamine changes in rat brain are different for convulsions induced by metrazol, by picrotoxin or by strychnine The suggestion of Darrow and perhaps, Toman that hypersynchronism in petit mal is related to decreased neurone activity and to unconsciousness, in contrast to the overactivity of grand mal, points to another possible dichotomy

I shall not go further into the problem of cortical and subcortical position of the pacemaker Both loci are clearly possible, action initiated in one may spread to the other (if repetition gives sufficient summation) return again, and reverberate throughout pretty much all of the cranial nervous system as McCulloch and Jasper have made clear Nevertheless these interconnections and reverberations are not necessary for the development of seizure activity — witness Jasper's most recent evidence of this by separating thalamus and cortex — and an exaggeration of the essentially automatic activity of individual neurones as such thus remains very much part of the picture How much a continuous spread along cortex depends on the fiber feltwork and how much on volume-conducted currents is not yet clear McCulloch mentioned DC potentials of 50 mV produced by strychnine and Dr Libet and I have seen swings of 50 mV with this drug and half as great ones, associated with negative spikes in slowly-spreading depression

I found myself fascinated by the evidence of the Montreal workers for a center of consciousness in deeper masses say the diencephalon which could be inactivated by the spread of the seizure process to it Whether such a center for consciousness will withstand the erosion of time and experiment better than its predecessors did remains to be seen, but at the moment I am gripped by a vivid mechanical picture Extensive activating fiber paths do spray out from the diencephalon to all parts of the cortex Activity of this deeper region can apparently bring in one or another cortical zone or can cut them all out with attendant evocation of particular psychic manifestations as in the hallucina-

tive memories or diplopic illusions of the temporal lobe or the paraesthesias and motor discharges of the Rolandic area So also does normal consciousness and attention wander about with illumination or darkening of current perceptions and remembered experience

The picture that has seized me at the moment is that of the cathode ray iconoscope From the deeply-buried electron gun (the unexplained drives of normal or excessive activity of the diencephalon) the electron beam (active diencephalon-cortical paths) is directed by controlling plates (impulses playing upon the conscious center') to the tube screen (cortex) Here it illuminates a region with an intensity depending on its current voltage and on previously deposited charges on microscopic droplet condensors (cortical neurones) As the beam scans this surface partial or complete pictures emerge depending on current conditions and past residues as the diencephalon impulses similarly scan the cerebral cortex shiffing attention about corresponding pictures flash in consciousness and give direction to simple sensori-motor coordinations I know as well as you that this is no more than a figure of speech and may do little good and much harm if taken as the basis for further experimentation — this completely omits for example the spread of activation within the cortex by continuity and very possibly without the use even of the neuropil — I mention it only because it may create some satisfaction in you as it has in me

A few final words on the basic disturbance The negative chemical evidence of Elliott and even more the positive clinical evidence of Penfield (on the activation of acquired neurone patterns) argue strongly against any important abnormality of particular neurones as the primary source of seizure activity That essentially normal neurones may however be raised to and kept in a state of excessive irritability is richly evidenced by Bronk s report[1] Changes in threshold of nerve cells and fibers resulting from an altered chemical milieu (as with altered calcium potassium acidity, carbon dioxide oxygen etc) from analeptic or convulsive drugs or their opposites neatly demonstrated in Toman s super duper response from temperature osmotic pressure or polarization changes even from magnetic fields are well known Such factors can hardly fail to be important in the genesis of discharges in brain as in nerve and are clearly indicated by such studies as those on ketogenesis and hydration

Last is the factor of the altered play of excitatory and inhibitory impulses upon these neurones of normal or altered irritability That this is of great importance is unequivocally shown aside from other evidence by the phenomenon of activity spread Whether this be primarily by propinquity through neural or other local mechanisms or by propagation to more distant fields the swelling wave of activity its spread with repetition and enhancement by strychnine proves that excessive stimulation as well as lowered thresholds is involved

Several speakers have pointed to the converse of increased positive excitation and the decrease of inhibitory control is certainly demanding of attention This might indeed be predominant in the production of an amnesic episode or unconsciousness and there is ample evidence for its importance in the respiration results of Bronk showing decreased oxygen usage with strong electric stimulation in the suppressor system of the telencephalon and the mesencephalon studied by McCulloch Magoun and others in the spasticities following anoxia pursued by Van Harreveld and those of Parkinsonism related to an inhibitory deficit by Wyke and his colleagues but the general impression of seizural phenomena remains that of excitatory overactivity rather than of disturbances of the inhibitory system Here indeed are many observations relative to seizures The ability of pacemaking neurones to recruit to them neighboring ones in the frog brain so as to produce large and perfectly synchronized electric beats the dash of strychnine-

[1] The contribution of Dr Detlev Bronk to this symposium was unavoidably delayed until the second issue of this Journal

evoked activity about the brain the shifting electrical dysrhythmias in man s cortex the reactivating neurone loops, all fit into the picture And, finally, there is the phenomenon of maintained central excitation indicated by Livingston's studies of causalgia by the work of Denslow on spinal reflex thresholds, and by that of Reynolds and Hutchins on referred pain

These all point to the possibility of setting up within the central nervous system a state of hyperactivity, a sort of physiological inflammation which is maintained in these cases by a continued rain of afferant impulses from the periphery When this bombardment is successfully interrupted for a period, the central inflammation subsides and the system returns to a state of normal activity and activability If such an active state underlies in part the seizures of epilepsy, kept up in this case more probably by centrally rather than peripherally originating stimuli it would easily explain the point emphasized by Lennox, that continued use of anti-epileptic drugs may not merely suppress the seizure manifestations but may also eliminate the seizure drive This is indicated by enduring improvement after discontinuing the use of a drug, a result not easily understood except by the interruption of a dynamic self-maintaining abnormal process

May I, in closing again congratulate the participants in this symposium on the truly impressive progress and understanding of epilepsy which they have exhibited to us in their own findings and their analysis of those of others I predict that the published record of this symposium in the new journal *Electroencephalography and Clinical Neurophisiology* will become a reference landmark in this field and I hope that such a session as this will help redirect the interest of electroencephalographers from the simple description of pen wiggles to the dynamic analysis of the beating neurones which generate these

THE CENTRAL EFFECTS OF RHYTHMIC SENSORY STIMULATION

V J Walter and W Grey Walter
Burden Neurological Institute, Bristol

The conventional EEG is a record of the *spontaneous* electrical activity of the brain Whatever may be the origin and function of the spontaneous rhythms it is certain that very few of the factors which affect them are under the observation or control of the experimenter or of the subject Usually only the effects of opening and closing the eyes of overbreathing and of changes in blood sugar are recorded Sometimes the influence of drowsiness and drugs can be investigated but the range and variety of methods cannot be compared with the scope and sensitivity of the organ studied It is not surprising therefore that the EEG has given unequivocal answers only to clinical problems characterised by the persistent or paroxysmal abnormalities associated with gross organic lesions or epileptic seizures The more subtle and transient variations between normal individuals and the features presented by psychiatric disorders escape notice or have to be dismissed because their importance could only be estimated if a detailed continuous assessment of the general state of the subject were possible Attempts to correlate EEG changes with other variables have been fruitful though limited by technical difficulties it is relatively easy to record changes in autonomic balance or total lapses of consciousness but very hard to devise a method for displaying fluctuations in the subjective state One encounters the familiar difficulty that the measuring device itself influences the variable to be measured

Instead of merely extending the field of passive observation it is possible to give EEG studies a more nearly experimental character by providing a controlled sensory stimulus and recording its effect upon both the EEG and other variables It is well known that stimulation of any receptor results in an electrical discharge in the cortex In animals this phenomenon has been used to evolve a physiological topography of the receiving areas (e g Adrian 1941 Marshall 1941 Marshall, Woolsey and Bard 1941) and even in man with electrodes on the scalp Dawson (1947a) has been able to measure the electrical response evoked in the sensory cortex by electrical stimulation of sensory nerves in the limbs These effects are too small to be seen with ordinary EEG techniques presumably because only very restricted cortical areas are activated by stimulation of a single sensory nerve the effects of more generalised peripheral stimulation do not seem to have been studied In Dawson s experiments the stimuli were either single at intervals of one sec or paired The effects of prolonged rhythmic stimuli have not so far been published but each of Dawson's subjects reported a change in the quality of the subjective sensation when the interval between the shocks was between 70 and 100 m secs A similar interval was found optimal for facilitation of the exaggerated response which was observed in a patient with myoclonus (Dawson 1947b) In this case single electrical stimuli or stretching of a muscle evoked brief myoclonic jerks while prolonged stimulation resulted in a generalised convulsion These results suggest that the destiny of a series of afferent volleys in the CNS depends in some way upon the interval between them or upon their group frequency

Stimulation of other receptors gives even more convincing results particularly when a very large group of sensory units can be excited simultaneously and rhythmically for then the central electrical response is correspondingly larger and the subjective reports more assured The ear and the eye present the best opportunities for such experiments for the whole basilar membrane

or retina can easily be stimulated in its own mode thus avoiding the difficulties inherent in the use of electrical stimuli with high amplification

The visual system is unique and peculiar in many respects, since the experimental section of this paper deals almost exclusively with photic stimulation the mechanism of sight-transformation should be considered in more detail To construct an adequate image of the light picture falling on the retina the receptor and central mechanisms must transmit information regarding brilliance, position shape and movement In addition some animals have colour vision and some also binocular stereoscopy Data on the essential parameters can be conveyed only by frequency modulation of impulses in the optic nerves and spatial projection on the cortex Clearly, whatever may be the central mechanisms which de-modulate and integrate these signals they are likely to be particularly susceptible to interference by rhythmic stimuli since the normal relation between an ordinary visual stimulus and the frequency pattern of the afferent discharges must be a most subtle and delicate one Considering these complexities the visual system would be the last to choose for experiment were it not that, in the first place it is easy to provide maximal and uniform light stimuli and in the second, the cortical projection areas are large and relatively accessible For these reasons the cortical response to light stimuli has been studied intensively, both in lower animals (Bartley 1934, 1937, Bishop and O'Leary 1936 Gruicksank 1937, Dubner and Gerard 1939, Fisher 1934, Halstead Knox and Walker 1942, Halstead Knox, Woolf and Walker 1942, Jasper 1936, Kornmuller 1932, Livanov 1938 1940, Livanov and Petrova 1938, Livanov and Poliakov 1945, Marshall Talbot and Ades 1943, Walker, Woolf Halstead and Case 1943, 1944 Wang 1934 Woolf, Walker Knox and Halstead 1945) and in man (Adrian 1943 1947 Adrian and Matthews 1934 Bertrand Guillain and Mazars 1945, Case 1942, Durup and Fessard 1935 Goldman Segal and Segalis 1938, Loomis Harvey and Hobart 1936, Monnier 1949, Toman 1941 Walter and Dovey 1947, and Walter, Dovey and Shipton 1946) The Clinical applications of this method have been studied only recently (Gastaut Roger and Gastaut *1948*, Walter 1946 1948, Walter and Dovey 1947, Walter Dovey and Shipton 1946, Walter, Walter Gastaut and Gastaut 1948)

The early work suggested and later observations have confirmed that

1 The primary electrical response of the visual cortex to single flashes of light falling on the eye resembles that found in other sensory receiving areas that is, there is first a brief surface positive wave, followed by a slower and more variable surface negative variation and sometimes a series of positive and negative waves The surface-positive component is considered to be a sign of activity in the cortical afferents while the negative and other later components are more likely to be due to the evoked activity of the cortical neurones and to repetitive after discharges arising in the thalamic relays With scalp leads the amplitude of potential changes varies from less than one to more than 100 μV In these conditions there is inevitably some distortion due to the size of the effective electrode, but cortical electrodes yield records which are not greatly different except in size and subcortical exploration shows quite similar results

2 The latency of the response is surprisingly long — about 100 m sec, from this must be deducted the latency in the retina, leaving about 50 m sec for the retino-cortical delay (Compare Monnier 1948, 1949) Since the conduction time in the optic nerve cannot be more than a few m secs some quite protracted process must intervene between the appearance of the impulses at, say the geniculate relay and the cortical response, there is evidence of both temporal integration and spatial diffusion

3 When repetitive stimulation that is a flickering light is used the response varies with the frequency and other characters of the photic stimulus with the features of the

spontaneous resting rhythms with other stimuli and with the subject

4 The region of the cortex involved in the response is not always the same as that generating alpha rhythms nor is it always identifiable with the primary or other visual zones

5 Mathematical or automatic analyses of records obtained during flicker stimulation reveal that the response is actually compound in all subjects at all times the proportion of sub-harmonics and harmonics varying over a very wide range Many of the minor components can be located as separate entities others probably arise from the inherent waveform of the elementary response When the flicker frequency is steady analytical methods permit measurement of tagged evoked responses even when these are too small to be visible in the primary trace or are masked by random disturbances or spontaneous rhythms

6 Stimulation by flicker invariably produces illusory subjective sensations particularly when the visual field is uniformly illuminated and when the eyes are shut

7 In subjects with organic cerebral lesions the evoked response often shows localised abnormalities and in some epileptics electrical seizure patterns and clinical attacks can readily be induced by photic stimulation at a suitable frequency

This summary of the accepted observations on photic stimulation indicates that the method can provide data of considerable physiological interest and clinical value As an adjunct to conventional diagnostic electroencephalography flicker stimulation is now a routine in several centres but there are still many features which demand further explanation This communication deals with 1 The classification of normal and abnormal responses 2 The relation between evoked and spontaneous activity 3 The connection between evoked electrical responses and subjective sensations 4 The observed and theoretical relation between photic stimulation and induced pathological states

METHOD

Electrical changes were recorded with 4- or 6-channel balanced amplifiers driving ink-writing recorders Various sensitivities time-constants filters and paper speeds were used according to the nature of the experiment EEGs were taken from silver silver-chloride electrodes on the scalp connected in bipolar fashion In many cases records were also made of the ERG EMG and ECG as well as of respiration skin resistance and reaction times using suitable electrodes and transduction devices Light flashes were recorded from a photo-electric cell between the eyes of the subject In addition an electronic automatic analyser was used to provide a frequency histogram from 1 5 to 30 c/sec This is reproduced as a dotted line in some figures in a contrasting colour in others

Since the light-source used for these experiments generates large transient electrical and magnetic fields precautions were taken to prevent the appearance of artefacts in the records The discrimination factor of the amplifiers was kept well above 1000 the inter-electrode resistance below 3000 ohms and the subject was earthed below the ear Stimulus artefacts could easily be recognised since they consisted of very brief spikes exactly synchronous with the flash as registered by the photo-cell

The light source was a Scophony electronic stroboscope giving flashes of blue-white xenon light with a time-constant of 15 micro-secs The frequency could be varied from 3 5 to 25 flashes per second without change in duration or brilliance and to 100 flashes per second at a reduced intensity The peak intensity of the flash was about 88 000 candles It should be noted that this stimulus differs from those used by earlier workers whose rotating discs gave much longer flashes which diminished in duration as their frequency increased In the conditions of these experiments variations could be made not only in frequency but also in brilliance position apparent size colour and amount of pattern or detail visible by the

light of the flash Since changes in frequency and pattern had the most interesting effects only these have been studied in most cases The effective brilliance is difficult to estimate but since considerable reduction did not reduce the size either of the ERG or of the cortical response it was assumed that the stimulus was supra-maximal In most experiments the effect of opening and closing the eyes was studied, closing the eyes naturally changes the brilliance, colour and pattern of the stimulus, but control experiments with neutral and colour filters showed that even with the eyes shut the intensity was still maximal and the degree of reddening insufficient to alter the ERG As a rule the lamp was fixed a few centimetres from the subject's face so that its light filled the whole of both visual fields

The records were taken with the subjects supine and close to the experimenter in a moderately light room Their eyes were photopic When possible they were asked to report any unusual sensations during the recording and were interrogated afterwards about their impressions of what they had experienced In clinical subjects particularly a close watch was kept for any involuntary movements

As well as the response to stimuli extended records were taken of the resting EEG, particular attention being paid to the characteristics of the alpha rhythms

In some experiments an electronic trigger circuit was used, specially designed by Mr H W Shipton This device contains frequency selective squaring and differentiating stages through which a standard pulse is derived from any desired component of any channel of the EEG amplifiers This pulse is used to trip integrating circuits which, after a time controllable by the operator, provide further pulses to fire the stimulating lamp and any other stimulus source, the two stimuli being also adjustable in their relation to one another In this way a flash can be generated in any desired time relation to either an evoked or spontaneous electrical change A further long delay circuit ,provides for stimulation at lower frequencies down to one per sec , but ensures that each stimulus still falls at any desired phase of the selected electrical rhythm or transient, The circuit details and application of this device will be described elsewhere

MATERIAL

Several hundred normal and clinical subjects have been examined some on scores of occasions Their ages varied from six weeks to seventy years The group of normal subjects included a wide variety of personality types Some were studied daily to follow the effects of mood changes, some hourly to observe the influence of hunger and fatigue An attempt was made to classify some of the subjects according to their habitual imagery A few submitted to more extensive psychological testing

The greater part of the clinical material was made up of epileptics and patients complaining of some sort of attack there were also cases of cerebral tumour and trauma as well as patients with behaviour disorders and various psychiatric disturbances

RESULTS

Since the observations are distributed over rather a wide variety of parameters, description of them may be clarified by first enumerating the principal variables These fall into three groups the features of the spontaneous resting EEG the evoked electrical responses and the other physiological and psychological effects of stimulation

Resting EEG For brevity the familiar Greek letter labels are used but not as a substitute for quantitative description The alpha rhythms are defined as rhythmic activity at 8 to 13 c/sec in the parieto-occipital region diminished by visual activity and mental alertness The term theta rhythm" is sometimes used to describe activity at 4 to 7 c/sec but only when *its association* with cortico-basal circuits can reasonably be inferred Delta rhythms are considered as slow discharges below 4 c/sec associated with dystrophy degeneration damage early develop-

ment and deep sleep Transient discharges are usually called slow or fast spikes

Since frequency analysis and other methods (compare Cohn 1948) have shown that the alpha rhythm' is nearly always compound this phenomenon is usually referred to in the plural Analytical data on other forms of activity are described according to whether there is evidence of their individual existence As explained elsewhere (Dawson and Walter 1944, Walter 1946) a complex waveform may be the result either of instrumental synthesis (the accidental superimposition of a number of discrete phenomena on a single trace) or to the inherent properties of the active structures The dilemma can be resolved either by spatial analysis or by experiments designed to alter some of the possible components and not others The elementary example of instrumental synthesis is the diphasic nerve action potential in which the two components can be separated either by further separation of the electrodes or by injury to the nerve fibre under one of them Similarly the monophasic action-potential spike of a single fibre may be an example of inherent limitation since no physiological procedure significantly alters its form It should be noted that while the compound nature of a waveform can be proved if the components can be altered independently of one another failure so to alter them is inconclusive until every conceivable experiment has been made

When the shape of a rhythm or discharge with a complex analysis was invariable and independent of electrode position it is described in terms of its form (for example spike or saw-tooth') When on the other hand the components revealed by analysis could be separately identified or when the form in the primary trace was different in different channels or in different conditions more emphasis is placed upon the analysis

Most of the resting records of the normal subjects were within the normal range but some adults showed theta activity comparable in amplitude with that of the alpha rhythm Since the experiments were primarily concerned with visual stimulation the records were divided into three groups 1 Those with little or no alpha rhythms even with the eyes shut and attention relaxed 2 Those with alpha rhythms easily blocked by mental activity and opening the eyes 3 Those in which the alpha rhythms tended to persist during mental activity and even with the eyes open This functional classification seemed more interesting than one based on measurement of alpha activity during constant conditions though such measurement is easy with automatic analysis (compare Golla Hutton and Walter 1943)

As will be seen later the evoked response as well as the spontaneous activity is greatly affected by opening and closing the eyes The visual system is the only part of the whole sensorium which can voluntarily be isolated from stimuli and as Adrian (1943) has pointed out the mechanism for opening the eyes is closely linked with those which maintain attention and consciousness There are many curiosities in the relationship however, for though closing the eyes is an essential preliminary to sleep and may even induce sleep when the rest of the organism does not particularly require it many people think better with shut eyes and visual imagery is usually more vivid without the competition of real stimuli Since the eyelids are by no means opaque the effect of closing the eyes in a bright light is mainly to eliminate detail from vision though reddened sufficient light penetrates to arouse a sleeper and changes in intensity are readily appreciated

Whatever the theoretical significance of these facts they must be considered in describing and classifying the effects of photic stimulation since the spontaneous and evoked potentials are bound to be superimposed in the record

Among the records from the clinical subjects were included nearly all the familiar types of abnormality Most varieties of seizure pattern were represented as well as the features associated with organic cerebral disease (Compare Walter Hill and Wil-

liams 1948) Particular attention was paid to the location of any abnormal discharge and to its responsiveness to stimulation, as in the case of the normal alpha rhythms

THE EVOKED ELECTRICAL RESPONSE

Examination of the primary traces and analyses provided the following information about the electrical responses 1 Amplitude 2 Frequency 3 Latency 4 Polarity 5 Waveform and harmonic content 6 Spatial distribution 7 Relations to other activities 8 Regularity, constancy and changes with other factors

While the first six of these variables were easily and automatically recorded those in the last two groups were much more difficult to evaluate The elementary response in the occipital region varied from less than one to more than 100 μV In a proportion of the subjects therefore the response was invisible in the primary trace but in all cases at some stimulus frequency an indication of it was observed in the analytical spectrum When visible in the primary trace the elementary occipital response was not difficult to identify since it had a fairly constant latency of about 100 m sec, followed the frequency of the stimulus over a range of at least two to one, and at stimulus frequencies of below 6 f/sec, had a distinctive polarity, waveform and location in each individual though there was considerable variation of these last three factors between individuals This is not surprising since the human visual projection areas are folded into the mesial surfaces of the hemispheres in such a way that their electrical projection on the occipital scalp must be variable and may often be inverted In several subjects, even the analysis failed to disclose any evoked response when both electrodes were over the occipital region of one hemisphere, but when one electrode was on the occiput a centimetre or two from the midline and the other in the central region on the opposite side, the evoked response appeared at moderate amplitude Exploration of this sort suggested that the generating dipole equivalent to the evoked response was radially orientated and at some depth below the occipital convexity Occasionally the first phase of the evoked response as recorded with scalp electrodes, appeared to be surface negative, suggesting that the superficial electrodes were seeing the projection areas as it were, from within Some of the experiments designed to locate the equivalent dipole suggested that some of the very variable secondary discharges which follow the elementary response are not orientated in the same way, and may represent local cortico-cortical interaction

It is likely that topographic variations may well account for many of the differences observed between individuals but they cannot be responsible for the variations in the same individual from time to time

In many cases and conditions the response is complex and it is often difficult to decide whether a change in the records during stimulation is due to the appearance of a primary evoked response mixed with spontaneous activity to some effect upon the spontaneous rhythms or to an indirect influence on a more remote mechanism undetected in the resting records Interpretation is particularly difficult in the case of responses evoked at frequencies other than that of the stimulus Usually, these are at sub-harmonics or harmonics of the fundamental flash rate, but Livanov (1938 1940) and Livanov and Petrova (1938) have reported that mathematical analyses of records from animals during photic stimulation reveal augmentation of resting rhythms whose frequency is near to but not necessarily exactly that of a harmonic of the stimulus frequency, together with suppression of components at adjacent frequencies There is certainly evidence in some cases that a spontaneous rhythm can be augmented even when its frequency is not a precise fraction or multiple of the stimulus rate and there is also a tendency for such rhythms to "pull-in" after a time There are also cases in which a spontaneous rhythm, usually an alpha rhythm, appears to resist pulling-in and even pulls away from its original frequency when that coincides with the stimulus rate

The regularity and consistency of the response itself increased during the first few minutes of the examination both in normal and neurological subjects. Anomalous and paradoxical effects in normal people tended to subside after the first few minutes but abnormal responses often became more intense. There is evidence therefore of short and long term facilitation and recruitment and, conversely, of habituation and fatigue. It was possible to identify some of the factors promoting these effects. In some cases the blood sugar level seemed to play an important part and in many spontaneous changes of mood seemed to correlate best with the observed variations. Some of the most striking changes in the records from normal subjects were seen when the subject reinforced a sensation elicited by the stimulus, whether pleasant or disagreeable, from his own memory or imagination. In these conditions a reverberating system was often established leading to marked augmentation of the indirect or secondary responses and of the subject's experiences. Conversely, voluntary inhibition of the evoked illusory sensation often attenuated the electrical response. Mental activity involving visual imagery generally diminished the evoked response as well as the alpha rhythms during stimulation at frequencies within the alpha band.

In clinical subjects the evoked responses covered an even wider range but most of the characteristic abnormalities were in the indirect or secondary effects rather than in the elementary response. In cases with well defined lesions of the visual pathways none the less the elementary evoked response was often asymmetrical, the components at the fundamental frequency being diminished while those at harmonic frequencies were increased. Even in grossly pathological cases the influence of the factors enumerated above could often be detected.

THE PHYSIOLOGICAL AND PSYCHOLOGICAL EFFECTS

Apart from the simple sensation of flicker the subjects had experiences in one or more of the following categories:

1. Visual sensations — in characters not present in the stimulus, that is (a) Colour, (b) Pattern, (c) Movement.

2. Simple sensations in modes other than the visual mode: (a) Kinaesthetic (swaying, spinning, jumping, vertigo); (b) Cutaneous (tingling, pricking); (c) Auditory (rarely); (d) Gustatory and olfactory (doubtful); (e) Visceral (probably connected with (a)).

3. General emotional and abstract experiences: (a) Fatigue, (b) Confusion, (c) Fear, (d) Disgust, (e) Anger, (f) Pleasure, (g) Disturbance of time sense.

4. Organised hallucinations of various types.

5. Clinical psychopathic states and epileptic seizures.

The subjective sensations and somatic effects varied over a wide range but correlated well with the amplitude, frequency and location of the evoked responses.

In most subjects the onset of a particular type of illusion or hallucination was preceded or accompanied by a characteristic alteration in the electrical response. When the sensation was primarily visual the electrical change was in the occipital region and was usually an augmentation of the response when the frequency was close to that of one of the alpha rhythms — not necessarily the dominant one. When the sensation was related to a non-visual sensory system the response was in the region where that system is cortically projected, the occipital response in these conditions often being diminished. Emotional and autonomic disturbances were usually correlated with augmented response at 6-7 c/sec. from the parieto-temporal region.

The interconnection between spontaneous or voluntary and evoked images and feelings has already been referred to.

For a few experiments two light sources were used simultaneously with independent flash frequencies. The records produced were too complex to be dealt with here but the hallucinations described by some subjects were of a character so compelling that

Fig 1

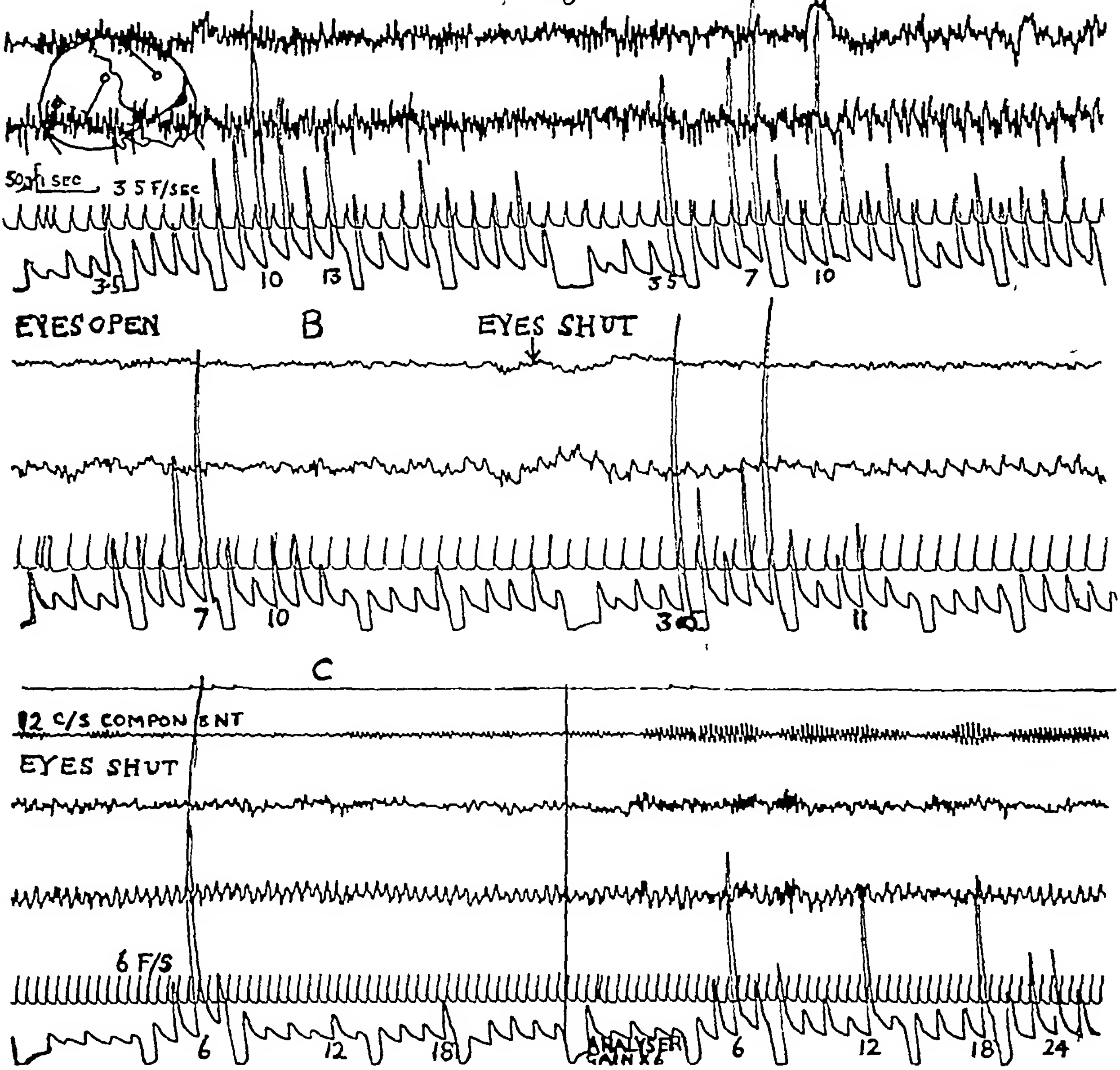
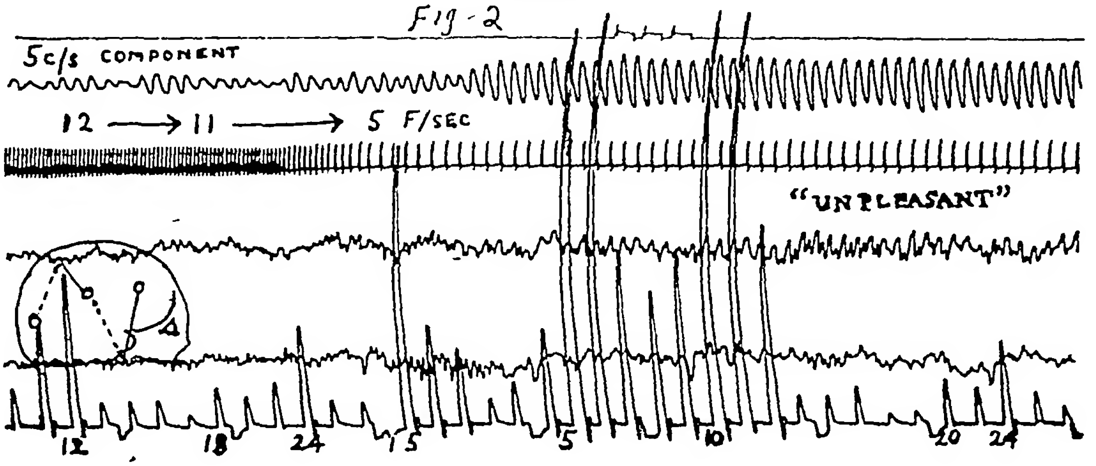

EYES SHUT
A
OPEN
3 5 F/SEC
35
10
13
35
7
10
EYES OPEN
B
EYES SHUT
7
10
11
C
12 C/S COMPONENT
EYES SHUT
6 F/S
6
12
18
ANALYSER GAIN x 6
6
12
18
24

Fig 2


5c/s COMPONENT
12 ⟶ 11 ⟶ 5 F/SEC
"UNPLEASANT"
12
18
24
15
5
10
20
24

one subject was able to sketch them some weeks later

In clinical cases most dramatic results were obtained in patients with a history of seizures Pathological effects were also induced in people with a family history of attacks but no personal record of any sort of fit The two most common objective disturbances were rhythmic myoclonic jerks at the frequency of the stimulus or one of its subharmonics, and the usual outward signs of a petit mal attack In the majority of cases in whom violent myoclonic jerks were regularly induced there was no history of myoclonus but only of major convulsions Myoclonic jerks have not as yet been observed in any cases whose only complaint was of minor attacks

The foregoing survey of the range covered by the three principal groups of variables can best be supplemented by a more detailed consideration (A) of the differences between individuals in constant conditions and (B) of the variations in given individuals with induced and spontaneous changes

A The main correlations with the differences between normal individuals were 1 Spontaneous or resting EEG features 2 Age 3 Personality type

The differences between normal and pathological subjects were of course greater than those within the normal range

A 1 Spontaneous or resting EEG features

Alpha components Some subjects with very large steady alpha rhythms of a persistent type showed almost no evoked response with the eyes shut and in these the component at the second harmonic was often greater than that at the fundamental frequency, this proportion was maintained when the eyes were open though the amplitude of all components was then increased In most subjects of this type response at frequencies below 8 f/sec was larger than that at higher frequencies (Fig 1 A) At the other extreme, subjects with little regular alpha activity usually exhibited an evoked response only with the eyes shut (Fig 1 B) It is important to note that in spite of the reduction in effective brilliance closing the eyes augmented the evoked response more in these subjects than did merely placing a diffusing screen before the open eyes In this condition the response contained a very large proportion of second harmonic In the intermediate group with classical responsive alpha rhythms there were usually signs of augmentation of the response and interaction with the spontaneous activity often at a frequency near that of one of the alpha rhythms

The same effect was observed in subjects with persistent alpha rhythms and an apparently similar one in subjects with no alpha rhythms at all This suggests that the appearance of resonance or driving may occur in two ways In the cases with marked alpha rhythms the augmented response in the alpha band was often shown by analysis to be due to addition of the evoked and spontaneous potentials in the recording system whereas in the subjects with no resting alpha rhythm this explanation cannot be adequate and it must be supposed that a neural mechanism with selective and resonant characteristics

Fig 1

A Analysed record from subject with persistent alpha rhythm Stimulation at 3 5 f/sec Analysis refers to second channel Note increase of response on opening eyes and large component at second harmonic

B Similar record from subject with little alpha activity Electrode positions gain speed and analysis same as in A Note increase of response on closing eyes and harmonic ratios

C Similar record from another subject with little spontaneous activity Note that in the first half analysis applies to centro occipital regions channel III in the second to fronto central ones channel II The analysis gain was increased six-fold during the second half Channel 1 shows the activity at 12 c/sec selected by one of the analyser circuits

Fig 2

Evoked responses in subject with considerable resting theta activity Analysis applies to channel III in which the fundamental and second harmonic components can be seen

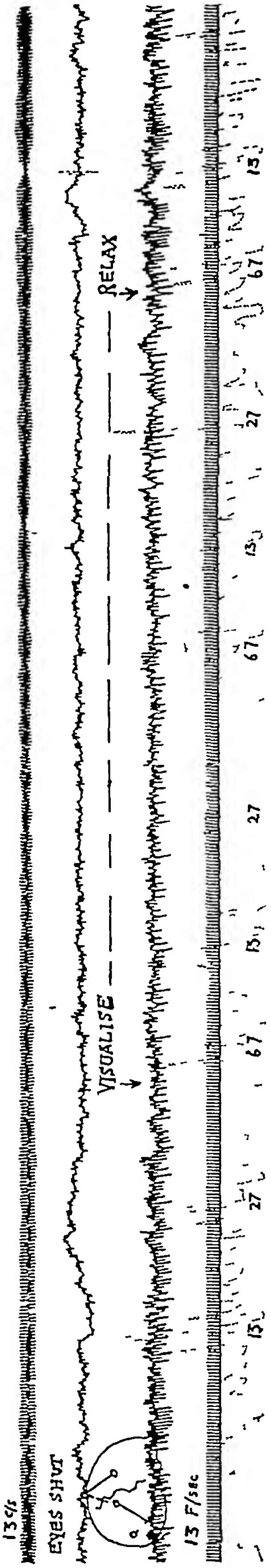


Fig 3 Analysis of effect of unwelcome visualisation upon evoked response Note decrease in fundamental and increase in subharmonic responses

was excited by the rhythmic stimuli In subjects with little spontaneous activity analysis showed that even when the response was regular and comparatively pure in the occipital regions, harmonic components could be detected in remote areas Fig 1 C illustrates this effect in a subject whose resting analysis showed little rhythmic activity even at the frequencies easily evoked by stimulation This phenomenon which is associated with many of the anomalous and unexpected results of photic stimulation, certainly occurs also in subjects with prominent alpha rhythms but in them it is more difficult to distinguish from instrumental summation

Theta Components Since the theta rhythm is a prominent component of the juvenile EEG correlations with this feature are bound up with age However a few of the normal adults displayed an unusual amount of theta activity in the resting records mainly in the parieto-temporal region These subjects were peculiar in various ways A rigorous psychiatric analysis was not available but the results of Rohrschach tests and tactful observation suggested that the main character common to all of them was some sort of immaturity or ingenuousness In these subjects the spontaneous theta rhythm was augmented during emotional stress Photic stimulation evoked elementary responses up to 8-10 f/sec above the average size and the chief secondary effect was augmentation of the theta component at stimulus frequencies of 5-7 f/sec or the harmonics, 10-4 f/sec (Fig 2) The subjects usually volunteered that they found stimulation at these frequencies particularly disagreeable not because of any visual sensations but rather because it produced a feeling of irritation and vague discomfort This state was susceptible to exacerbation by additional affective stress which also augmented the response in the theta band

In one subject, for example (Fig 3) stimulation at 12-14 f/sec evoked activity both at the fundamental frequency in the occipital region at the second harmonic and at the sub-harmonics 6-7 c/sec, the last named

being very much smaller during relaxation. When the subject was asked to visualise a painting which she disliked the 6-7 component was considerably augmented and the response at the fundamental frequency and second harmonic attenuated; their proportions however were reversed. The change was sufficiently large to be seen clearly in the primary trace as well as in the analysis and the subject reported a feeling of revulsion and exasperation. This effect gradually subsided with repeated trials.

activity whose evoked response contained components in this band, usually in the upper range 7-8 c/sec, described their sensations as pleasureable, with marked kinaesthetic illusions (Fig 4). When these sensations were most vivid the theta component was most prominent in the parietal region. A similar response in the theta band could occasionally be evoked in some subjects not merely by flicker at that frequency or harmonic frequencies but also by changing the frequency rapidly from say 10 to 16 flashes

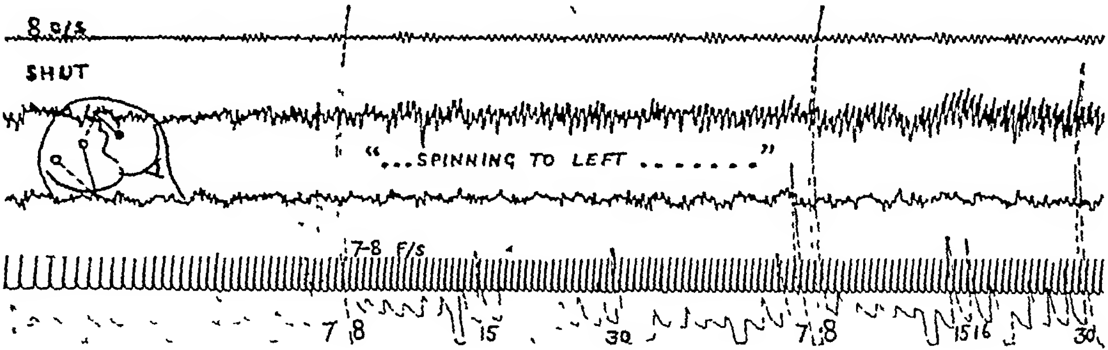


Fig 4

Fronto parietal response from normal subject associated with spinning sensation. This effect lasted for only a short time.

A response in the theta band of frequencies in adults was not limited to those with such components in their resting records. The few adults without spontaneous theta

per second and back again (Fig 5). When a theta response occurred in these conditions the subject could recognise it subjectively as a brief unpleasant sensation. This sort of

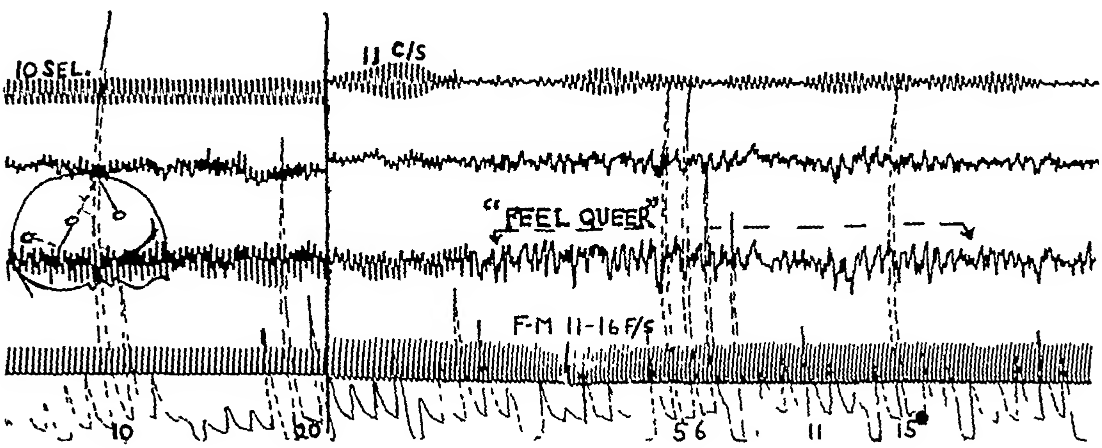


Fig 5

Production of response at 5 6 c/sec by frequency modulation of stimulus between 11 and 16 f/sec. The first section of record shows the response of the same subject to steady stimulation. The top channel indicates when the response frequency is at 11 c/sec during modulation. Note that the slow components are projected toward the anterior regions.

effect tended to wear off after several repetitions

In clinical cases many patients with resting theta components, particularly young epileptics exhibited a dramatic augmentation of this feature during photic stimulation within this frequency band The response was often very selective This group contained a large number of specially interesting individual cases some of which will be described elsewhere, two illustrate some of the more uncommon effects The first, a boy of 7 with a personal and family history of epilepsy had a complex resting record with components as shown in figure 6A with frequent small spikes The largest and most continuous component was at 5 c/sec from the posterior regions As the figure shows photic stimulation greatly augmented this component The effect did not develop instantly but re-

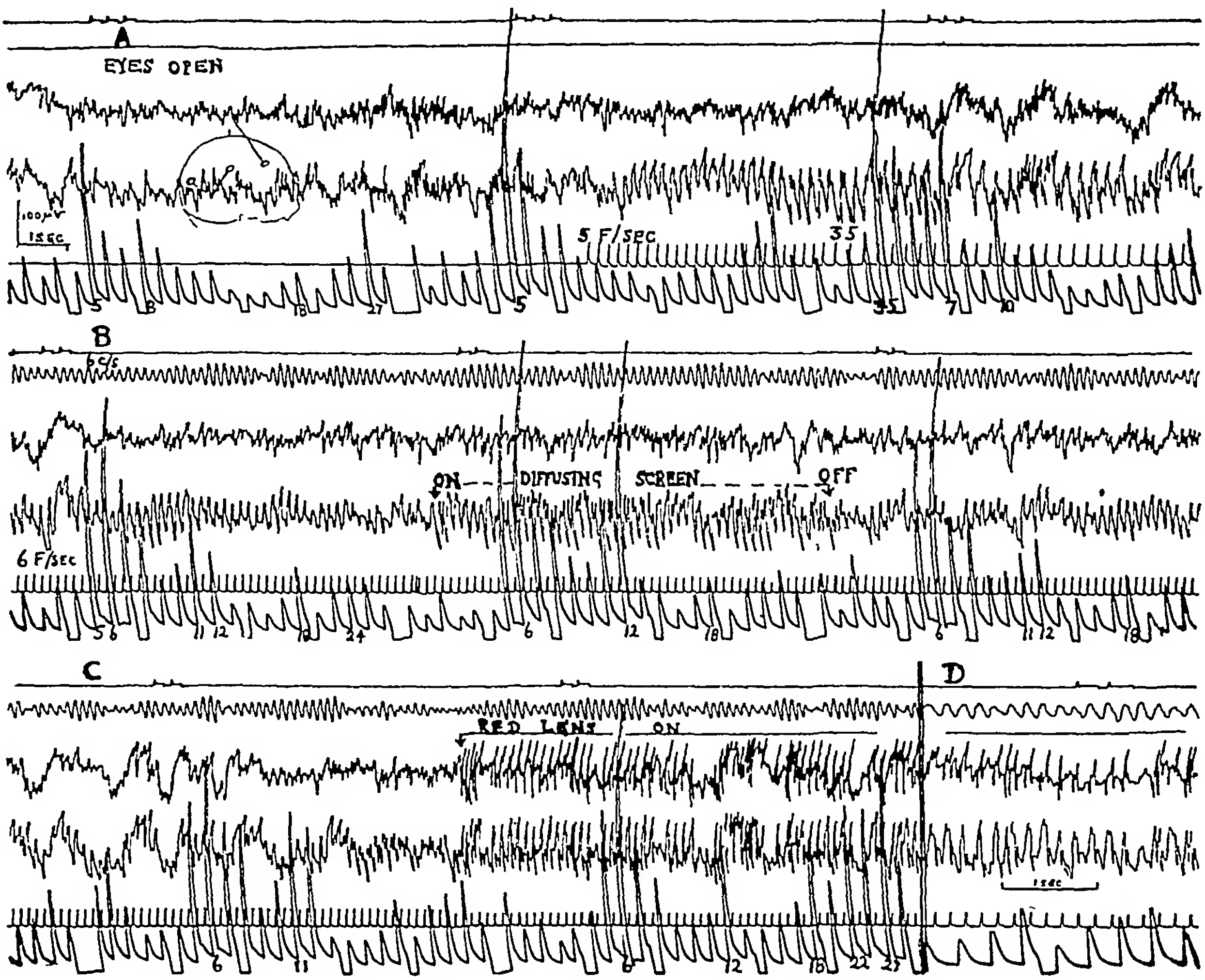


Fig 6

A Record from epileptic boy First section shows resting record with analysis of centro occipital channel showing major component at 5 c/sec Stimulation starts at 5 f/sec and is later reduced to 3 5 f/sec Note harmonics at the lower rate

B Analysis of effect of placing a diffusing screen before the eyes Analysis is of the fronto central region Note increase in harmonic content

C Analysis of effect produced by interposing red lens filter Analysis is of fronto-central region Note harmonic and high frequency activity associated with spikes

D The same taken at higher speed Note relation of spikes to other components in the two channels

quired three or four stimuli for its evolution Stimulation at lower frequencies also evoked a large response but this often subsided Restoration of the stimulus to 5 f/sec showed a return of the 5 c/sec response From the figure it can be seen that during stimulation at 3 5 f/sec the evoked response was mainly at 7 c/sec and was about equal to the spontaneous 5 c/sec rhythm while at 5 f/sec the response was many times larger and contained relatively few harmonics in the posterior regions though further forward there was more activity at 10 and 15 c/sec A very strange phenomenon was observed in this patient when a diffusing screen was placed between the light and the eyes the response was affected as shown in figure 6B In the posterior regions the amplitude of the response at the fundamental frequency was somewhat augmented and the proportion of second harmonic increased several fold, the change being seen in the primary trace as a transformation from asymmetrical square or sawtooth waves into monophasic spikes The anterior leads were affected even more the response at the fundamental frequency being increased about 20% but that at the second harmonic more than three fold The harmonic components appeared to be located at the electrode common to the two channels i e in the right central region When the screen was removed the record immediately returned to its original character No such effect was produced by closing the eyes An even more dramatic change was observed when instead of a white diffusing screen a large red tinted lens made of gelatin was interposed before the eyes (Figs 6C and D) The effect of this was to colour the light scarlet but the intensity was not greatly reduced since the light was concentrated by the lens With this stimulus the response became extremely spikey due to the appearance of many harmonic components in the central region During the first third of a second the response was usually a burst of spikes at twice the stimulus frequency and this doubling occurred from time to time during the exposure to red light Many other high frequency components besides harmonics were observed in the analysis No unusual subjective or clinical disturbances appeared during these experiments

The second patient in the abnormal theta group was a girl aged eight with a history of frequent myoclonic epileptic episodes and major fits There were signs of pyramidal involvement but no cranial nerve disturbance The condition appeared to date from encephalitis at the age of three but the major seizures had only been present for one year The resting records showed frequent large spikes most prominent in the right frontal region with a focus in the right central area These were accompanied by bursts of delta waves the whole complex appearing at a smaller amplitude in the left hemisphere Twitching and jerking movements frequently occurred at the same time as the spikes There was also a large rhythmic bilateral occipital discharge at 5-6 c/sec, this was completely blocked by opening the eyes Several hundred records were taken from this patient the results were too intricate and varied to be described in detail here During photic stimulation the most intriguing finding was of sharp spikes at an amplitude of over 200 μV, in the motor zone which built up gradually when the stimulus frequency was at any multiple of 2 5 f/sec particularly 5 f/sec and the eyes were shut (Fig 7A) Unlike the case previously described it was apparently necessary for the spontaneous 5 c/sec rhythm to be fully developed and for the flash to be at exactly this or some numerically related frequency (Fig 7C) Coincident with the appearance of spikes were brief muscular jerks particularly of the left arm (Fig 7B) It was possible to tune in the stimulus simply by holding the patient s hand while the frequency was varied When stimulation was maintained for more than a few seconds in these conditions the jerking spread to the other limbs and finally developed into a major convulsion Once the jerking had become generalised it could not be terminated by removing the stimulus but when the stim-

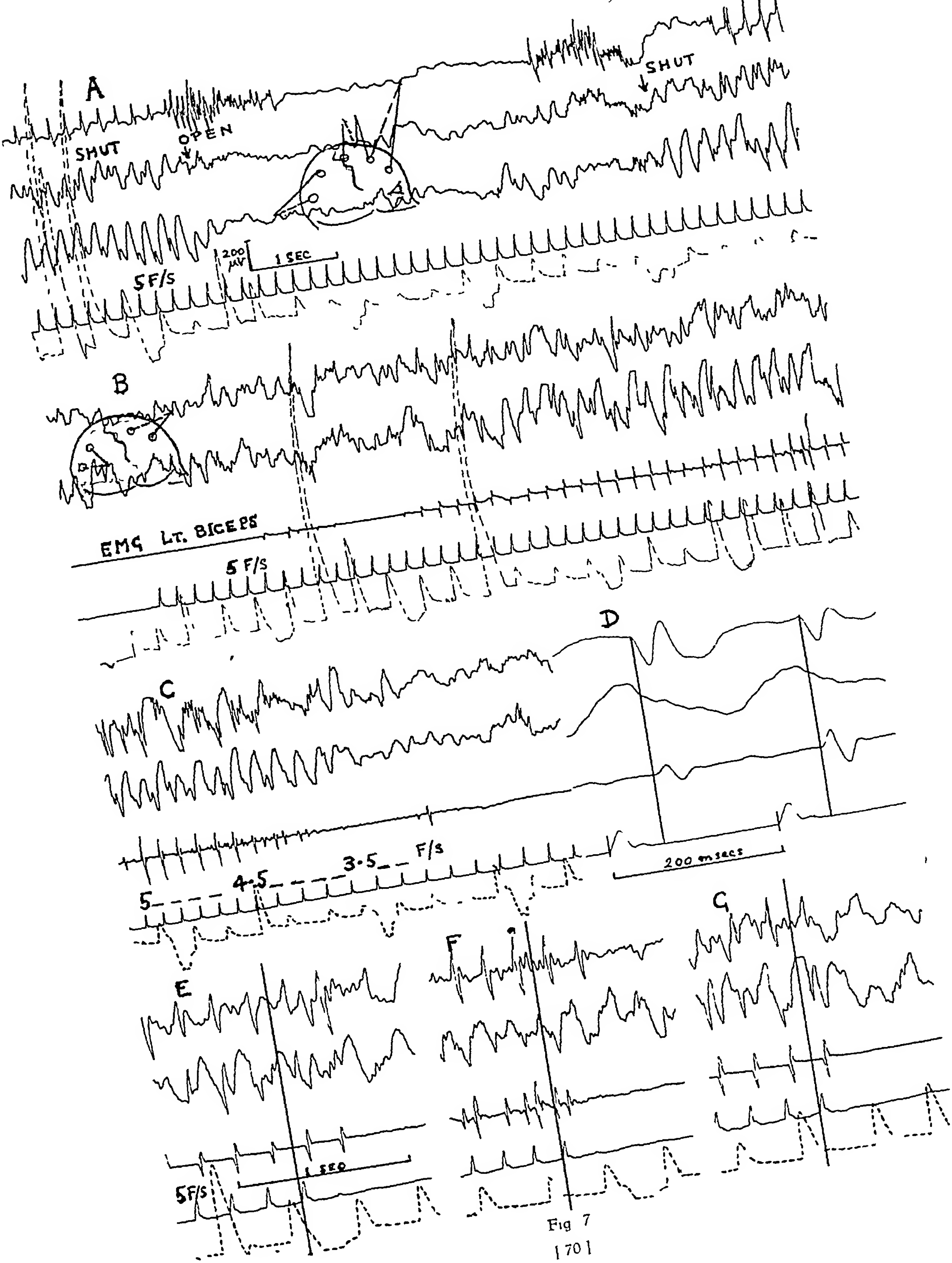

A
SHUT
OPEN
SHUT
200 µV
1 SEC
5 F/S
B
EMG LT. BICEPS
5 F/S
C
5
4.5
3.5
F/S
D
200 msecs
E
1 SEC
5F/S
F
G

Fig 7

lation lasted a shorter time, the jerking and frontal spikes subsided with the extinction of the light or opening of the eyes, on some occasions there was a short after discharge The time relations between the flash the cortical spikes and the action potentials of the arm muscles were measured on high speed records (Fig 7D) The latency of the cortical spike was 65 ± 5 m secs The muscle action potentials occurred synchronously with the cortical spikes ± two or three m secs If the normal retinal delay 50-60 m secs is deducted from the latency only 20 m secs at the most is available for the effect to spread from the optic nerve to the motor cortex and to the limb muscles This time is very much less than the latency of the normal elementary occipital response so that it seems unlikely that the leak from the optic to the motor systems was through the visual cortex Now augmentation of the spontaneous 5 c/sec rhythm was an essential preliminary to the pre-motor and peripheral discharge The slow increment and high selectivity of this process suggests that it was one of true resonance in which case the rhythm would settle down with a constant phase relation to the stimulus and would not show sudden changes either of frequency or amplitude when the stimulus was either changed in frequency or cut off altogether Such behaviour was in fact observed in a large number of records and can be seen in some of those in figure 7 This explanation implicates the parieto-occipital wave in the genesis of the cortical and motor discharges the flash being merely an accessory in pushing the wave up to a size where it can discharge adjacent structures This is conceivable if the 5 c/sec rhythm represents activity in the parieto-pulvinar-occipital circuits from which potential fields might radiate far enough to raise the excitability in say the dorso-medial region of the thalamus If these mechanisms were the only ones it would be expected that the motor discharges also would persist for at least one or two waves when the stimulus was cut off but this was observed clearly in only one experiment out of several hundred (Fig 7E) On several occasions the frontal spike alone persisted for one wave (Fig 7F) but far more frequently the frontal and peripheral discharges ceased immediately the flash was stopped (Fig 7G) Further evidence that the simple explanation is inadequate was obtained by stimulating at higher frequencies at 7 5 and 10 f/sec the 5 c/sec wave was still augmented but the frontal and muscle spikes tended to follow the frequency of the stimulus appearing usually in bursts at the stimulus frequency on the falling phase or trough of the occipital wave as conventionally recorded This means that the augmentation of the 5 c/sec rhythm was not an adequate cause of the spikes but merely lowered the threshold of the pathological process responsible for them for a part of every half cycle during which time the afferent volleys in the optic tract were able to detonate the final explosion In other words the unique and intricate connections between eye closing flash frequency and time relations in this case seem to be due to the two-fold effect of the afferent volleys from the eye progressive amplification by

Fig 7

Responses of myoclonic patient discussed in text

A Effect of opening and closing eyes Note regular frontal spikes which disappear when eyes are open
B Gradual developement of frontal spikes and muscle action potentials
C Disappearance of cortical and muscular discharge with change of stimulus frequency from 5 f/sec Note frequency doubling just before muscular discharge disappears
D High speed record to show time relations between flash (fourth channel) muscle discharge (channel III) occipital wave (channel II) and frontal spike (channel I)
E Effect of stopping stimulus The only occasion on which a cortical and muscular after discharge were observed
F Effect of stopping stimulus Note after-discharge in cortex but not in muscle
G Effect of stopping stimulus One record out of many in which no after discharge occurred

resonance of the spontaneous rhythm and regular triggering of the charge which the first process had primed

An attempt was made to separate some of the hypothetical components of this effect The photic stimulation on one occasion was continued throughout and after a major convulsion which it had evoked For two and a half minutes after the end of the convulsion no muscle action potentials or jerks were evoked by the stimulus but the cortical spikes though somewhat attenuated, returned immediately the seizure discharge was over At three minutes both phenomena had entirely recovered On another occasion a convulsion was induced by electrical stimulation and the effects of photic stimulation were again recorded during and after the seizure During the first minute after the end of the convulsion both muscular and cortical activity were entirely absent At two and half minutes the muscle action potentials had returned almost to their original size but the cortical spikes remained extremely small for nearly ten minutes The only difference observed between the two sorts of convulsion was that the photically induced one appeared to evolve from the fusion and spread of myoclonic jerks while that induced by electrical stimulation began with the usual tonic phase It is tempting to infer from these observations that the tonic phase ' the electrically induced seizure involved a cortical mechanism exhaustion of which delayed the reappearance of the frontal spikes but did not fatigue the parapvramidal structures discharging to the periphery Similarly, it might be considered that the photically induced seizure was essentially an excessive interaction between thalamic centres leading to exhaustion of the presumed parapyramidal efferents but not unduly straining the cortical metabolism

Beyond the scope of this paper is the effect of drugs which was also investigated

That this case was more than a pathological curiosity is suggested by the results obtained in two identical twins both suffering from myoclonic epilepsy of the Unverricht type Both these patients developed large frontal spikes and violent jerks during photic stimulation and the detailed characteristics were the same as in the last case whose illness had come on suddenly after an encephalitis

Delta components Since the only normal conditions in which these components are prominent is in very young children and deep sleep it is not surprising that when they were found in the resting records the evoked responses were very small or absent At low stimulus frequencies particularly in children of about ten years of age, the evoked elementary response resembled a delta rhythm in its time relations, but it would be confusing to describe it in those terms since it has none of the correlations enumerated above (Fig 8) It is difficult to account for the extremely large protracted elementary response found in some normal children Its appearance is as though the classical primary response were drawn on an enlarged scale Some adults showed similar features but the amplitude was not as great

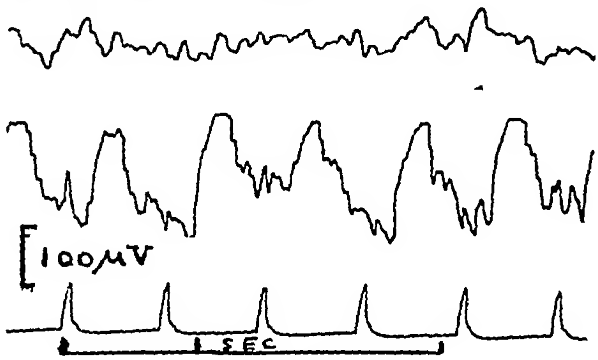


Fig 8

Elementary occipital response from normal child aged ten to indicate the upper limit of size Compare with Fig 1

Some of the appearances in cases of organic brain disease have already been mentioned briefly Whereas the presence of delta activity in the resting records even when focal is only an indication of some indeterminate cortical disturbance the characteristics of the evoked response can be used to trace faults in the visual pathways and association areas in considerable detail For

example the delta rhythms due to trauma usually subside in a few months after the injury and it is often difficult to tell from records in chronic post traumatic states whether the absence of delta activity indicates recovery or atrophy

tion showed a marked asymmetry On the normal side the response to 8 f/sec for example showed a response at 8 c/sec with a component about one third the size at 24 c/sec On the side of the lesion the proportions of these components were reversed that

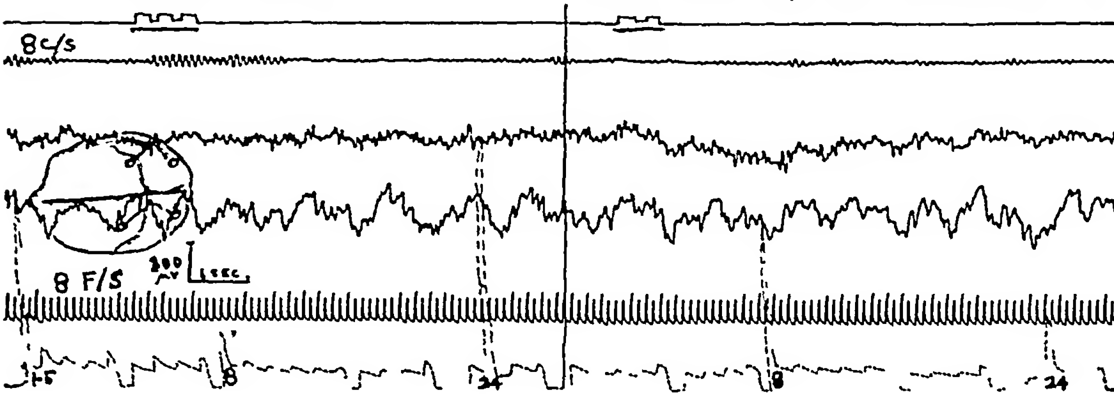


Fig 9

Analysis of responses from a case of trauma Analysis of first half from abnormal second half from normal side Note difference in harmonic proportions

The records in figure 9 were taken from a man of twenty-eight years who had had a severe gunshot wound through the left hemisphere one year earlier The delta activity was still prominent on the side of the injury and there was a residual paralysis of the

at 24 c/sec being about six times that at the fundamental frequency suggesting involvement of the visual association pathways on that side

A disproportion between harmonics and fundamental was a frequent finding in or-

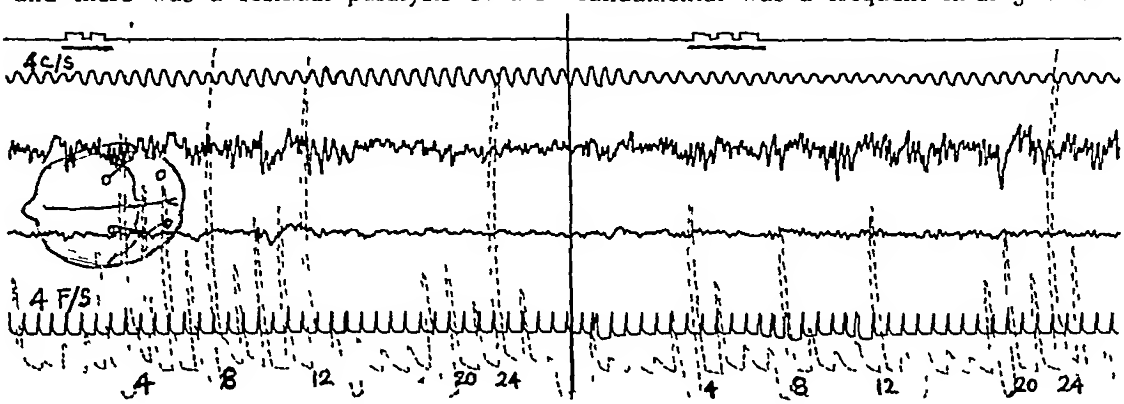


Fig 10

Analysis of responses from child with atrophy First half of record from normal second half from abnormal side Note harmonic proportion

right arm and leg Although the delta discharge was evidence of persistent cortical disturbance it was uncertain as to what extent the deeper structures might be affected Analysis of the response to photic stimula-

ganic cases even when the resting records showed no visible abnormalities In cases where one hemisphere exhibited some relatively slight abnormality and the other side little rhythmic activity of any kind in the

resting records photic stimulation sometimes revealed an unusual preponderance of high harmonic responses on the apparently more normal side An illustration of this is given in figure 10 which was taken from a child of ten who had had a right hemiplegia since birth and two attacks during the three years before the examination There was ample evidence of cerebral agenesis or atrophy on the left side The resting records showed complex rhythms between 5-11 c/sec on the right side all augmented by closing the eyes and almost complete electrical silence on the left side Photic stimulation evoked responses from the right hemisphere at frequencies between 3 and 18 f/sec, the harmonics at the low stimulus frequencies being rather smaller than the fundamental but extending up to the sixth On the left side analysis showed a small response at fundamental frequencies below 18 f/sec The accompanying harmonics were equal to or larger than the fundamental component and the sixth harmonic in particular was often twice the size of the fundamental

SEIZURE PATTERNS

In this group there were no normal subjects and the patients were only those who complained of some kind of seizure Of the records taken from patients with this complaint during rest and overbreathing 80% contained some abnormal feature but only about 30% of the abnormalities were diagnostic seizure patterns Photic stimulation evoked anomalous responses in 40% of those with abnormal resting or overbreathing records but in none of those with normal records

The evoked abnormalities seemed to fall into two main classes

1 *Typical wave and spike discharges* similar to those which occur spontaneously These were evoked most easily in patients whose spontaneous seizure patterns arose or were most prominent in the posterior regions In such cases mostly children photic stimulation was most effective when the flash frequency was at the fourth or fifth harmonic of the fundamental wave and spike rhythm usually between 12 and 18 f/sec (Fig 11) In some cases a seizure pattern could be induced by stimulation at the fundamental frequency but these were rare and all presented signs of organic disturbance as in the patient with myoclonus already described Most of the patients in this first category were children complaining of frequent minor seizures but some had had major convulsions Both the clinical accompaniments and the persistence of the induced seizure patterns depended upon the length of time for which stimulation was continued after the disturbance had arisen If this time was less than about one second there was no apparent change in the patient's state, the spike component disappeared immediately and the slow waves subsided in a second or two (Fig 11) When stimulation was continued for longer after the seizure pattern had developed the patient usually became unresponsive with upturned eyes and fluttering eyelids, in cases with frequent spontaneous wave and spike discharges which were easily augmented and protracted by photic stimulation cessation of the stimulus did not always ter-

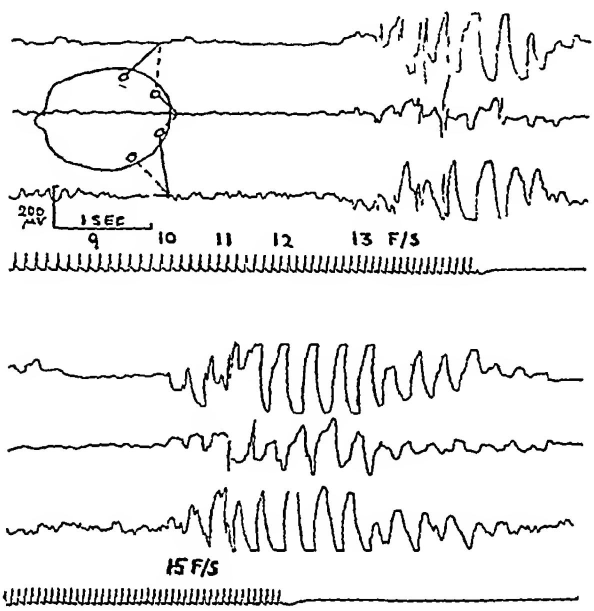


Fig 11

Two occipital larval seizures induced in an epileptic child by stimulation at the frequencies indicated No clinical accompaniments

minate the seizure discharge The onset of the seizure pattern was usually delayed for some seconds after the commencement of stimulation and usually developed from a smaller discharge of square or saw-toothed waves

In those patients whose resting seizure patterns were diffuse or frontal the effective frequency was more critical and usually had to be fished for quite diligently In these cases the stimulus frequency was not the *only important factor the phase-relations between the stimulus and some component of the spontaneous rhythms appeared equally critical* Although as in the other cases the effective frequency was usually between 12 and 18 f/sec the rate had to be varied rapidly in order to achieve phase-modulation and held the moment the response appeared The importance of the phase relations between the stimulus and the spontaneous and evoked rhythms was confirmed by application of the electronic trigger circuit already described judicious use of which increased the number and persistence of seizure patterns evoked in refractory subjects The frequency phase and harmonic relations between the components selected for triggering and the flash are complex and obscure In one patient consistent results were obtained only when the trigger was set to near the crest of every seventh wave of the 8 5 c/sec component as displayed by the trigger (Fig 12) The effective component for triggering was not always an occipital one but was usually prominent in resting analyses The first sign that a seizure discharge was imminent was often an augmentation of the preferred triggering component

2 In the second category of abnormal evoked responses were records showing a gradual build up of *irregular slow waves with occasional spikes* whose relation to the slow components was variable If photic stimulation was continued in these cases the spikes frequently became the dominant component particularly in the more anterior regions and the effect culminated in a shower of high voltage spikes without waves at the stimulus frequency This phase was usually accompanied by violent myoclonic jerks without disturbance of consciousness and in spite of the jactitation the patients did not complain of any disagreeable sensations but volunteered that the experience made them feel 'shakey No typical wave and spike patterns were observed in the resting or overbreathing records of these patients which were characterised rather by intermittent or paroxysmal discharges of moderate potential often of a spikey appearance, their analysis revealed a wide range of quasi-harmonic components The effective stimulus frequency was less critical than in the first group and bore no obvious relation to the resting components The evoked discharge rate was also unrelated to that of the spontaneous rhythms or of the stimulus until the frontal spikes appeared which were either at the stimulus frequency or a fraction of it Opening and closing the eyes had little effect upon the ease with which seizure discharges could

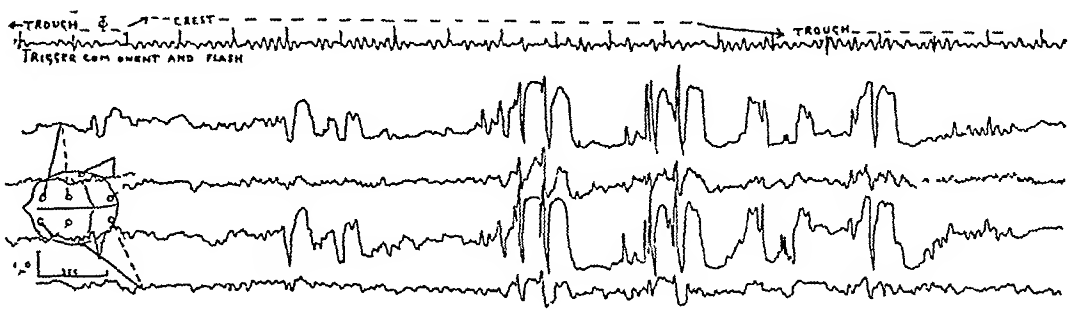


Fig 12
Frontal seizure patterns induced by stimulation of epileptic by means of trigger circuit Explanation in text

be evoked in these patients but at the onset of stimulation the spontaneous alpha rhythms were usually diminished (Fig 13A) and were also attenuated for a few seconds after the paroxysmal discharge even when the light stimulus had been removed All the patients in this group complained of major seizures, very few had minor attacks The patient whose record is shown in figure 13B was particularly interesting since after the stimulation he mentioned that it had made him feel exactly like he once had when cycling down an avenue with trees through which the sun was shining, he had suddenly realised that his cycle had come to rest but he had not fallen off and he was gripping the handle bars fiercely It seems likely that during the brief attack induced by the flickering sunlight he had stopped pedaling and thus changed the frequency of the stimulus, in so doing he had automatically terminated the attack This history is precisely similar to those recalled by Cobb (1947) and Gastaut (1948)

When the effective frequency for a patient in this group had been discovered the latency of the seizure response tended to diminish at each exposure until after six or seven trials the spikes and jerks appeared after only a second or so of stimulation (Fig 13C)

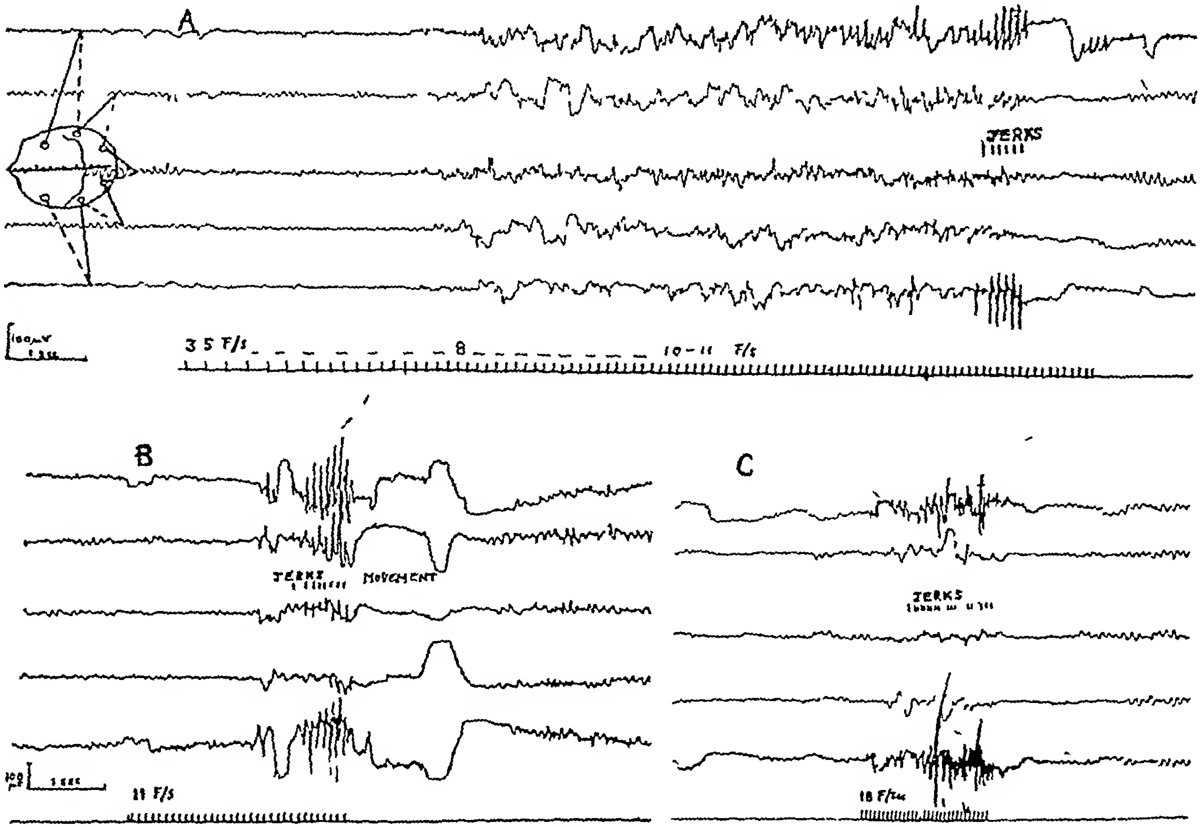


Fig 13

A Myoclonic seizure induced in epileptic by stimulation at indicated frequencies Note suppression of alpha rhythm by commencement of stimulus

B Myoclonic seizure induced in another patient Note synchrony between stimulus and frontal spikes

C Myoclonic seizure induced in a third patient This was the seventh in ten minutes Note short latency and complex asynchronous discharge

A2 The correlation of age with the individual variations has already been referred to in several places The connection is not a simple or invariable one however, and observations are still in progress Some normal children show larger and more regular responses than any normal adults but in most children below the age of six the response is

very small compared with the amplitude of the resting rhythms and may not be detected without analysis The small size of the elementary response in early youth contrasts markedly with the ease with which abnormal responses and seizures can be induced in young patients, suggesting that the pathological effects are not due to any unusual size of the evoked potentials in the visual cortex

Young children with small evoked responses are of course perfectly capable of interpreting visual stimuli but the size and complexity of the response may be related in some way to the richness of detail with which a stimulus is invested in the juvenile imagination

A3 The correlations of the evoked response with personality type and temperament are ineluctable but cannot be set down systematically until some universally acceptable human typology has been established, and its relation to individual EEG patterns has been worked out It has already been suggested (Golla Hutton and Walter 1943) that individual differences in the responsiveness and persistence of the alpha rhythms are correlated with variations in habitual mental imagery, since as has already been mentioned the evoked response also varies with these features of the alpha rhythm it is logical that some connection should be looked for between the different ways in which people think and the character of their evoked responses This is a laborious and baffling task some of the tentative inferences have been referred to elsewhere but the electrical observations are easier to classify than the psychological data which are rarely in a quantitative form In the meantime it seems clear that the evoked responses vary even more between individuals than do the spontaneous rhythms particularly in the way they are affected by other stimuli and internal physiological and psychological changes

B The variations of the evoked response in given individuals with induced and spontaneous changes are hard to classify without making spurious or arbitary distinctions which disregard the integrative and homeostatic functions of the CNS Some factors which have interesting effects upon the response to photic stimulation are certainly in the internal environment (i e the blood sugar level) others such as closing the eyes and apparently spontaneous changes in mood have both internal and external correlates Some such as variations in the light itself are truly external but when a trigger circuit is used even this becomes a part of the intricate network of retroactive circuits

In this communication there is space only for consideration of a few selected variables 1 Blood sugar level 2 Visualisation 3 Mood

1 *Blood sugar level* Both normal and clinical subjects exhibited more striking anomalies while they were fasting than when the blood sugar was at or above the normal level An example of this effect is given in figure 14 The patient was a man aged 34 who had been convicted for a series of sexual offences The resting records showed continuous diffuse theta activity at 5-6 c/sec and no alpha rhythms Photic stimulation while fasting revealed marked asymmetry of the evoked response particularly at 7 f/sec (Fig 14) On the right side there was a moderate sized steady response from the occipital lobe with few harmonics On the left side there was no clear response at any frequency, but the record became irregular with analyses showing increased activity in the low and high bands The examination was repeated half an hour after the ingestion of 50 gm of glucose using the same technique The asymmetry had then almost disappeared the evoked response being greatly reduced on the right side and the low and hiqh frequency activity diminished on the left

2 *Visualisation* The effects of mental activity have already been mentioned as one of the factors responsible for individual variations In some normal subjects the effect of visualisation on the evoked responses is even more regular and characteristic than it is on the spontaneous rhythms One subject whose

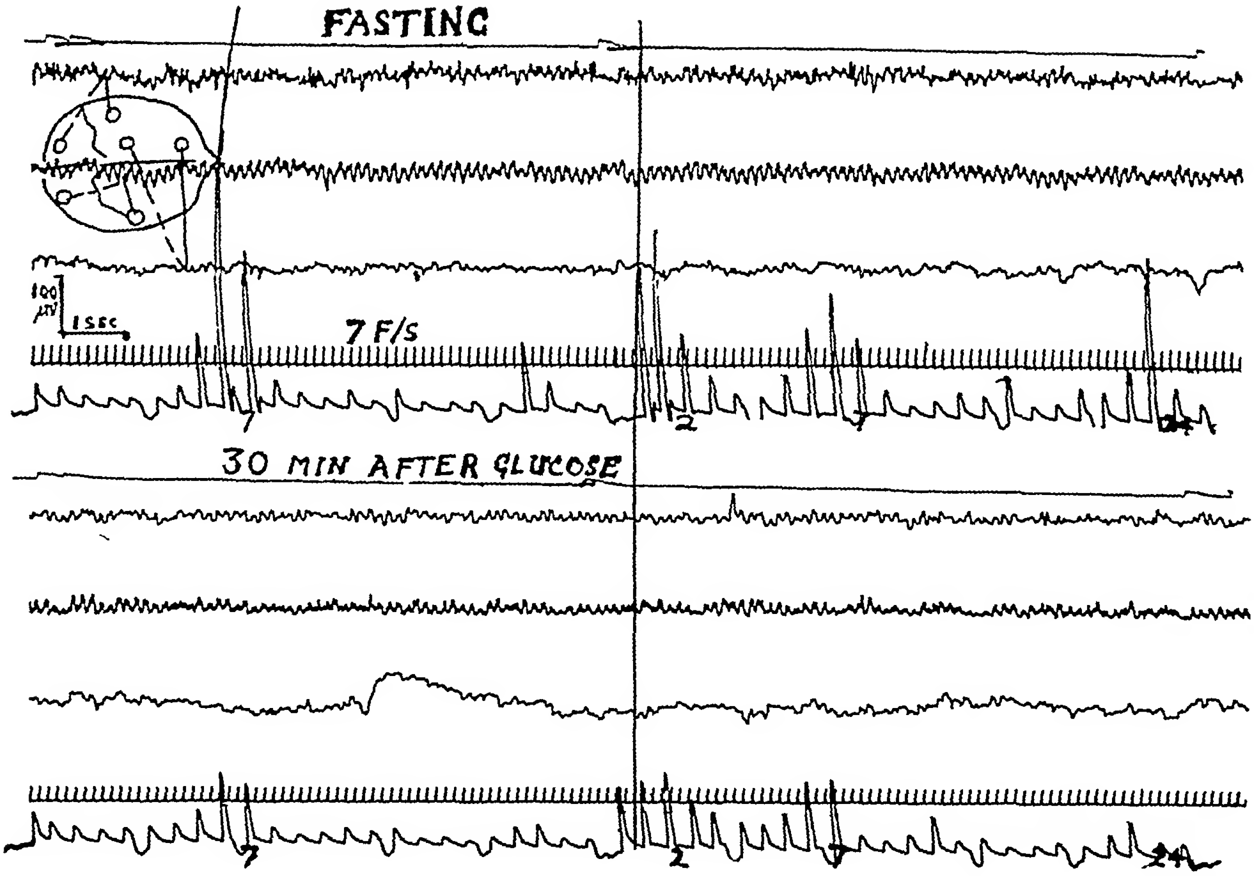


Fig 14

Effect of raising blood sugar upon asymmetrical response in a psychiatric patient In each record the first analysis applies to the right centro occipital and the second to the left centro-occipital regions

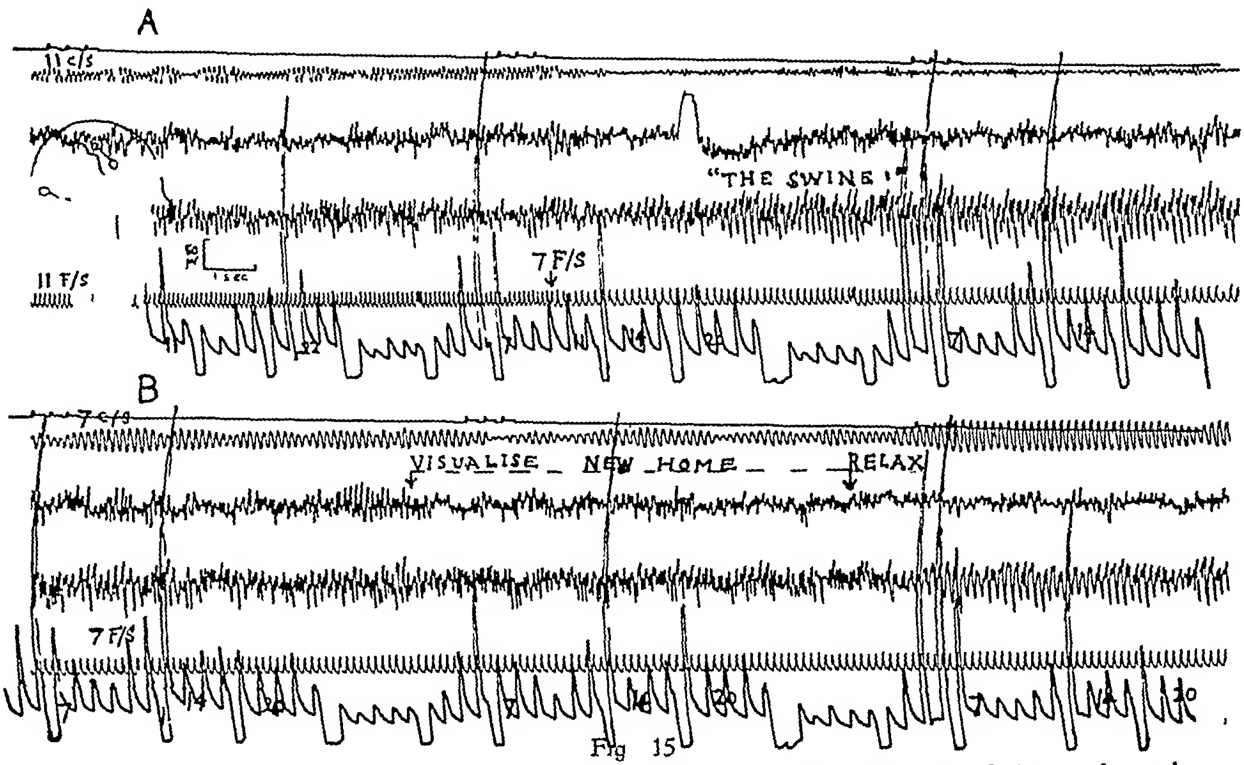


Fig 15

A Responses from normal subject at 11 and 7 f/sec The latter associated with feelings of revulsion Analysis is of the temporo-occipital region

B Effect of visualisation in same subject Note suppression of fundamental and its later augmentation during rest

alpha rhythm was at 11 c/sec and rather persistent even with the eyes open had a particularly large and complex response to stimuli at 7 f/sec There was a large component at the second harmonic for all stimulus frequencies When the stimulus rate was set to this frequency from another one he usually responded with an exclamation of disgust (Fig 15A) During stimulation at this rate he was asked to visualise a series of familiar scenes On each occasion the amplitude of the response at the fundamental frequency was approximately halved while that at the second harmonic was unaffected and the third harmonic was increased almost to the size of the fundamental (Fig 15B) A similar but less marked effect was observed when a red light was used for stimulation (Fig 6C)

It is interesting to note that a similarly high ratio of harmonics to fundamentals was observed in patients with lesions of the visual pathways there seems a possibility that the exercise of visual imagination may divert certain fundamental components of the visual afferents from the occipital cortex while in pathological cases other components at harmonic frequencies can be relayed to deafferented areas by other systems

3 *Mood* Changes in the evoked responses correlated well with fluctuations of mood even when no appreciable difference could be seen in the resting records The variation was principally in the harmonic and sub-harmonic components and effects found in non-visual areas One subject frequently exhibited at 5-6 c/sec when the stimulus rate was modulated between 11 and 16 f/sec (Compare Fig 5) This anomalous response was accompanied by a disagreeable sensation Whenever this subject was in a tense and irritable mood a similar response was obtained even when the stimulus frequency was slowly raised through 14 f/sec and the characteristic feeling was very marked (Fig 16A) When in a tranquil state on another day no such effect was observed (Fig 16B) The subject soon came to be able to predict accurately from introspection whether the response would occur or not

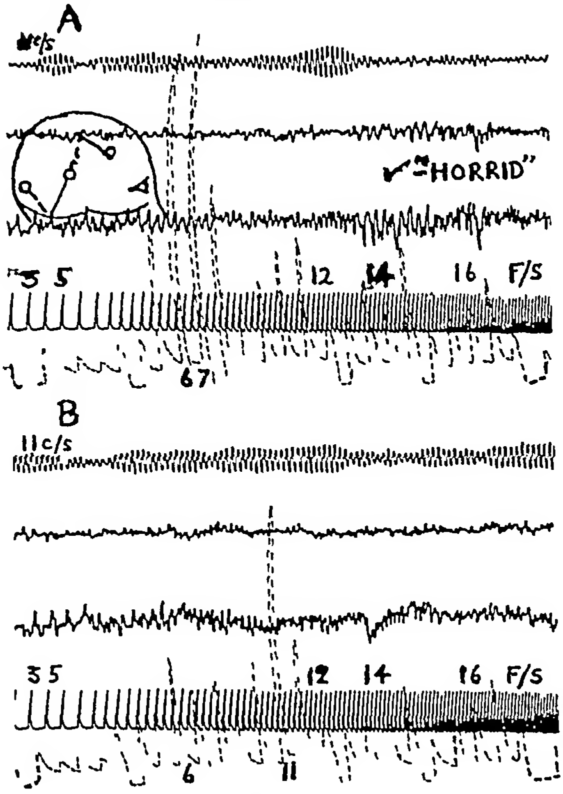


Fig 16

Records from same subject as figure 5

A Development of temporo occipital response at 6 7 c/sec as stimulus frequency passed through 14 f/sec Taken while subject was in irritable mood and associated with unpleasant feeling

B Record taken later with subject in cheerful mood No slow response and no unpleasant sensation Note suppression of 11 c/sec component as shown in top trace during first record and persistence in second

DISCUSSION

Before attempting to integrate or explain these findings the nature and fate of the signals arriving at the CNS during any rhythmic stimulation must first be recalled

As is well known volleys of impulses reaching the CNS from the periphery do not necessarily bear a simple or linear relationship to the physical conditions embodied in the stimulus In general differences n stimulus intensity are converted into differences in impulse frequency that is the receptors operate a system of *pulse frequency modula-*

tion The second important feature of peripheral transmission is that nearly always *changes* in stimulus intensity are transmitted rather than steady or absolute levels, this corresponds to a process of differentiation whereby rapid changes produce a greater effect than slow ones and the response to a sudden increase in intensity to a new steady level is signalled as a volley of impulses at a high initial frequency which declines exponentially to zero, even though the stimulus change may be maintained indefinitely

The advantages of this design are obvious — a much wider range of stimulus intensity can be handled by frequency modulation of unit pulses than could be imposed upon a scale of amplitudes, even supposing that a nerve fibre were capable of such modification Furthermore extreme sensitivity to changes in stimulus intensity can be achieved without blocking by high steady intensities It may be worth noting that similar advantages are gained by similar means in solving electronic problems for example by using differentiating couplings in amplifiers, and integrating circuits to transform wide variations of voltage into varying intervals between pulses

Whether in living or artificial systems such devices have interesting limitations as well as desirable properties One of the drawbacks is that transformation of this sort distorts the orginal stimulus signal to some extent and clearly can never add to the information it contained Thus both integration and differentiation are with respect to time and therefore a certain time interval must elapse before the transformation can be complete Further stimulus changes at different rates will be treated differently with the result that at low rates of change a maximum frequency of impulse discharge may coincide not with a maximum intensity but with a maximum rate of change of intensity while at higher rates frequency maxima will coincide with stimulus maxima Phase shifts of this sort are not usually of very great importance since the CNS introduces even larger distortions but it is instructive to consider how many familiar illusions fallacies, and ambiguities may have their origin in the confusion introduced by the differentiating and integrating components of the peripheral nervous system

It is often difficult to decide without careful experiment, whether a given effect is due to peripheral or central limitations most visual illusions for instance have both components An example of how the frequency modulating transducer in a receptor may generate misleading signals is illustrated in figure 17 In this experiment a preparation of the skin and dorsal cutaneous nerve of the frog was used A single touch receptor was stimulated by a glass micro-needle attached to a 100 c/sec tuning fork which was driven by an air-jet The nerve-trunk leading to the skin was laid on non-polarisable electrodes in an emulsion of paraffin and Ringer's solution in this way drying was prevented while at the same time the inter-electrode resistance was kept high Records of the action potentials in the nerve trunk were taken with a balanced amplifier Matthews oscillograph and moving mirror cam-

Fig 17
Action potentials in single fibre of dorsal cutaneous nerve in frog Stimulation of single receptor with micro needle at 100 per sec

era The maximal response of a single receptor of this type to a sudden maintained increase in pressure is a brief discharge containing about 100 impulses at a frequency declining exponentially from an initial maximum of about 200 per sec the time constant of the frequency decline is usually about 0 3 sec at room temperature However as the record in figure 17 shows, when the receptor is stimulated at 100 per sec even when the intensity of the stimulus is only just above threshold the discharge frequency follows that of the stimulus so that the nerve fibre transmits to the CNS a continuous stream of impulses at a frequency normally associated with the onset of a nearly maximal steady

stimulus. It is obvious that apart from rhythmic stimulation a persistent discharge of this type could only be maintained by the application of a stimulus increasing rapidly from near maximal to supra-maximal and even in this case the conditions for maximal discharge would exist only for a very short time. It is reasonable to infer therefore that as felt by the CNS the volley of impulses set up by the very weak but rhythmic stimulus would imply the existence of an inordinately intense and rapidly increasing pressure. It could be predicted that the response of the intact animal to a rhythmic stimulus of this sort would be exaggerated unless there is some other nervous mechanism whereby the fallacy could be revealed. This is borne out by observation for a frog stimulated in this way responds with a startled leap though it may be quite unmoved by touching the skin of the back in the ordinary way.

Rhythmic stimulation often evokes responses which are not merely quantitatively but qualitatively different from those associated with steady excitation of the same receptors. In human beings from whom subjective as well as objective information can be obtained the characteristic sensations and effects of tickling, stroking, rocking and so forth are too familiar to require description but it is important to bear in mind that the signals due to rhythmic stimulation of even a simple receptor appear to reach parts of the CNS which are inaccessible to impulses set up by non-rhythmic stimuli however intense. The sensation produced by mild faradisation of a sensory nerve is quite unlike that due to normal stimulation of the receptor related to the nerve. Weddell, Sinclair and Feindel (1948) have suggested that the specific character of certain painful stimuli may be due to a *simplification* of the impulse pattern which causes the afferent volley to be diverted from its usual route. Inevitably associated with this diversion is an increased latency not merely because of the longer route but also because it is the *persistence* of the afferent volley which is anomalous from the standpoint of the CNS the frequency may be well within the range of the usual discharge rate, but some time must obviously elapse before the fact of persistence can be established.

Some further matters should be mentioned. First since the CNS appears to be able to distinguish between a steady and a varying frequency[1] and is also able to de-modulate frequency variations to detect their implicit amplitude connotation we must expect that it will discriminate also between different steady frequencies set up by rhythmic stimulation but such discrimination will not necessarily provide any useful information about the nature of the original stimulus-signal and may indeed give rise to quite irrelevant though highly specific illusions. The next point is that as well as the properties already outlined most receptors exhibit some degree of fatigue during rhythmic stimulation. This is quite distinct from the adaptation or differentiation characteristic of the response to ordinary stimuli and has a longer time constant, put crudely it is more like the running-down of a battery than the discharge of a condenser since the response follows a long plateau before subsiding fairly rapidly to exhaustion. During the early stages the first sign of fatigue in the receptor is usually a tendency to discharge at every other stimulus so that the impulse frequency falls suddenly to half then later perhaps to other fractions of the stimulus rate as more stimuli are missed between discharges. The passage of time may therefore be marked by abrupt illusory changes in sensation.

Further complications are introduced when each of a series of rhythmic stimuli is sufficiently large or prolonged to generate a

[1] The mechanisms whereby the CNS discriminates between volleys at declining or variable frequencies and those at steady rates does not seem to have been identified but Mr H W Shipton has pointed out to us that a very simple analogy is familiar to radar engineers as a reflecting delay line in which pulses can be either augmented or neutralised when they occur at a steady frequency but are relatively unchanged when the frequency is varying. Delay networks with these properties would seem an inevitable feature of neural organization.

train of impulses at a declining frequency At some stimulus frequency and intensity the average discharge rate will be exactly twice that of the stimulus at another, three times and so forth though with larger or longer stimuli at lower frequencies the impulses will be irregularly grouped each group showing the characteristic die-away in frequency A record taken in these conditions looks rather like a slide-rule upside down

So far only single units have been considered, naturally many receptors are usually stimulated at the same time and the situation may consequently be complicated, but when brief, physically uniform stimuli are used, the volleys in a nerve trunk do not always differ very much from those in a single fibre

In the case of the ear and the eye still further complications are introduced In the ear, the presence of many sharply tuned vibration receptors demonstrates yet another mode of stimulus transformation, the scale of sound frequencies is converted into a spatial display which is carried right into the brain, with the consequence that the electrical discharges in the auditory nerve and projection area may summate to reproduce the original sound by a process of physiological analysis followed by instrumental re-synthesis — the well-known effect of Davis and Saul The effect bears no relation to the mechanism of hearing or pitch-discrimination for in a single nerve fibre — and presumably in a single cortical unit — loudness is conveyed by frequency differences as in other receptors Rhythmic stimulation of the organ of hearing as a whole can be accomplished only by using a sound stimulus containing components of supra-liminal intensity over the whole gamut of audible frequencies — in effect a steep fronted sound such as that produced by an untuned percussion instrument or an explosion Here again the specific effects of rhythmic sound stimuli are familiar and frequently exploited for various purposes

The operations which the eye must perform upon visual stimuli in order to convert them into frequency-modulated spatially displayed impulse volleys are more intricate than those in a simple receptor, the preliminary neural relays in the retina make photochemical, chemo-electrical and integration transformations so that the signals which reach the visual cortex contain information in five or six categories The integration effect was of course very prominent in the experiments described above for the duration of the stimulus was of the order of 10 microsecs while that of the ERG and presumably of the impulse volleys was nearly ten thousand times longer Furthermore, since the intensity of each stimulus was subjectively and objectively maximal the impulse frequency and density must have been maximal also for a short time, yet in spite of the brilliance of each flash the subjects were not dazzled after the stimulation nor did they describe vivid or persistent after-images This absence of long-term integration is probably attributable to the low average intensity — about 20 candles It seems likely that in spite of its high peak intensity the total energy in each flash was insufficient to cause much retinal adaptation so that only the short term integration and constant latency of the retina had first order effects upon the character of the afferent volleys, which would not resemble any normal signals until the stimulus frequency was such that the interval between flashes was about half the duration of each volley

As has been pointed out (McCulloch 1947 Pitts and McCulloch 1947, Walter and Walter 1949) the visual areas of the cortex whose function is to pass on afferent signals to the rest of the nervous system must be capable of changing yet again the co-ordinate systems upon which the signals are arranged It seems likely that one of the mechanisms by which this is done is represented by the alpha rhythms as scanning generators which convert the spatial pattern of excitation on the visual cortex into a code of impulses on a time base for transmission to other regions With steady or slowly chang-

ing illumination this system works well but if the brilliance fluctuates at a rate comparable either with the group frequency of impulses in the optic nerves or with the spontaneous rhythms the whole device would be thrown out of gear

However jamming by rhythmic signals would not shut the central visual mechanisms down The scanning generators would still function but instead of performing their routine space-time transformation they would relay volleys of impulses at some frequency related to the stimulus With large stimuli at low frequencies the relayed impulses would tend to be at a frequency which was at a high harmonic of the stimulus rate When the stimulus intensity was reduced and particularly when the field became more uniform that is when the eyes were closed the proportion of harmonics would tend to be reduced (See Fig 1B) The conditions for harmonic generation would be fulfilled most often when the scanning rhythm was already locked on some internal image the response would get simpler as the internal state became less involved At higher frequencies close to those of the scanning rhythms themselves similar conditions would maintain but a new effect would appear when the scanning mechanism began to lock on the afferent volleys The impulses relayed in these circumstances would be similar to those set up when the scanning generators were sweeping a regular projected pattern The receiving station would see such a pattern and it would change with frequency but the image would not be anything like the stimulus in fact it would not be related to the stimulus at all it would be a display of the scanning *raster* itself

If as seems probable similar mechanisms deal with signals from other receptors it follows that rhythmic stimulation in any mode is likely to produce impulse volleys at harmonic frequencies somewhere in the CNS, associated with specific illusory sensations The prominence of such effects with visual stimulation is probably due to the great extent of the cerebral excitation and to the richness of the association mechanisms It is these latter which determine the fate of the artificial secondary rhythms Many will certainly be quite meaningless and will be disregarded others, as we have seen will give rise to clear though irrelevant and illusory sensations Others again may happen to be synchronised with some other rhythmic mechanism functionally inaccessible to visual associations in the normal state In such conditions the remote mechanism may be jammed just as the visual one is with similar results A third rhythm may be corrupted and so on until the whole brain is pulsating in harmonically related modes This of course is precisely what happens in a seizure but no generalised seizures have yet been induced in subjects with no personal or family history of epilepsy Many of the records and sensations in normal subjects would be quite abnormal in the absence of photic stimulation but unless the patient is in some way predisposed the abnormality does not spread to more than two or three circuits with for the most part only subjective sensations Even in normal people the activity evoked in non-visual regions is real enough not only to be seen in the records but also to evoke appropriate somatic responses righting reflexes in those with kinaesthetic illusions autonomic changes in those with emotional disturbances for example In some way nevertheless the normal brain constrains the evoked rhythms often with the aid of the subject's conscious effort in banishing the phantom Even in some epileptics opening the eyes or mental concentration can change the conditions enough to break the chain reaction at its weakest link before the rhythmic stress has gone too far Once a certain proportion of the central circuits have been drawn in, no degree of concentration — not even stopping the stimulus — can break the feedback loop

The anatomical basis for these hypothetical processes can easily be surmised In some cases there was direct evidence of interaction between afferent and efferent circuits at a thalamic level in none was there any sug-

gestion of direct spread of activity for more than a few centimetres through the cortex From many other sources (Delgado and Livingston 1948 Droogleever-Fortuyn and Jasper 1947, Ward 1948, Ward and McCulloch 1947) there is evidence of similar effects in experimental animals during stimulation of thalamic centres and not far from these are the undifferentiated nuclei which seem to maintain the spontaneous rhythms (Dempsey and Morison, Morison and Dempsey 1943) Quite apart from the physiological function of the cortico-thalamic circuits, interaction between them is to be expected chiefly perhaps only, where they are in the closest proximity It is not the intricacy but rather the miniaturisation of the CNS which is its greatest weakness and the despair of *imitators*

The correlation between electrical observations during rhythmic stimulation and psycho-physiological studies, only briefly touched on in this communication, promises to be one of the firmest bridges between classical neurophysiology and the broader studies of animal behaviour Livanov and Poliakov (1945) have claimed that they can follow the formation of a conditioned reflex in the brain of a rabbit by using rhythmic conditioned and unconditioned stimuli During the pregeneralisation stage, rhythmic discharges at frequencies related to the stimuli appeared in both conditioned and unconditioned receptor fields, during the generalisation stage the evoked rhythmic activity was widespread and towards the end of this phase the conditioned reflex appeared usually accompanied by a sudden augmentation of the rhythmic response in the conditioned field When the reflex was established the evoked rhythms became smaller and appeared only in response to the conditioned stimulus All the details of classical Pavlovian conditioning are alleged to have their counterpart in the evoked rhythms

From the other side of the divide are numerous reports relating changes in the subjective response to photic stimulation and the effect of such things as practise stimulus pattern and simultaneous auditory stimulation (Knox 1945) There is also evidence of changes in the subjective impressions in neurotic states and endocrine disorders (e g Krugman 1947)

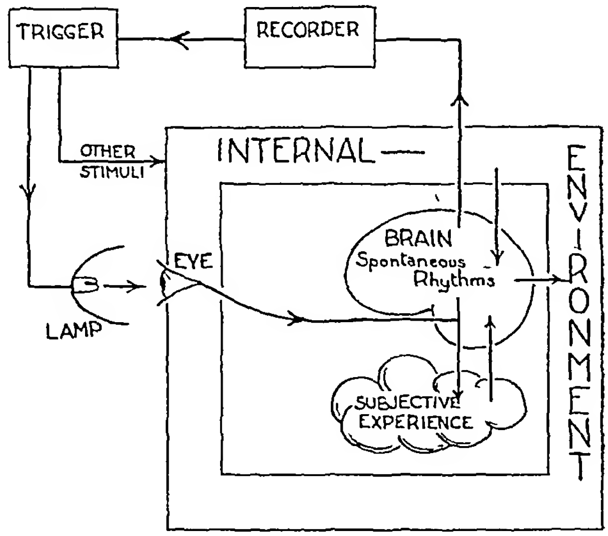


Fig 18

Some of the groups of retroactive networks suggested by the various experiments are indicated schematically in figure 18

The speculative top-hamper may be counterbalanced by a ballast of predictions Some of these were first made some time ago and have in fact already been partially confirmed but they still suggest interesting experiments 1 Any drug which increases the amplitude of a spontaneous rhythm should have a marked effect upon the response to photic stimulation whether the drug is usually classed as a convulsant narcotic or sedative The same should apply to fatigue and drowsiness 2 It should be possible to induce anomalous effects, including seizures in some cases by rhythmic stimulation of any receptor 3 Combined stimulation in two or more sensory modes should summate or neutralize according to the phase relations of the two stimuli 4 With appropriate psychological analysis and classification some correlation should be found between the features of the evoked response and some such character as originality or creative imagination

SUMMARY AND CONCLUSIONS

1 Records obtained during photic stimulation may be described in terms of the following components, any or all of which may be present at any one time or from time to time

A A series of discrete elementary evoked responses e g figures 1B and 8

B Fusion of evoked responses giving an accidental appearance of rhythmicity (first part of figure 5)

C Instrumental summation of evoked response and spontaneous rhythms (Fig 1A)

D True augmentation or driving of local rhythms at the frequency of the stimulus

E Augmentation of harmonically related rhythms in other areas

2 Differences between individuals are attributable in some cases to anatomical variations and correlate also to some extent with the character of their spontaneous activity with age and with differences in personality

3 Alterations in the response in given individuals are produced by somatic mental and emotional changes whether spontaneous voluntary or induced

4 Somatic mental and emotional changes can be induced in the subject by stimulation at appropriate frequencies

5 The above effects can interact with one another in both regenerative and degenerative fashion

6 Subjective visual effects are attributed to interference between rhythmic evoked responses and spontaneous rhythms at cortical and possibly thalamic levels

7 Anomalous (non-visual) effects in normal and abnormal subjects are attributed to interaction between the evoked activity and harmonically related spontaneous rhythms in other circuits at a thalamic level

8 Evocation of activity in non-visual circuits can be used to study their physiology and as an aid to diagnosis of some pathological conditions

9 Some theoretical implications of these findings are speculatively discussed

REFERENCES

ADRIAN E D Afferent discharges to the cerebral cortex from peripheral sense organs *J Physiol* 1941 *100* 159-191

ADRIAN E D Doyne Memorial lecture the dominance of vision *Trans Ophth Soc* 1943 *63* 194 207

ADRIAN E D The physical background of perception Oxford 1947

ADRIAN E D and MATTHEWS B H C The Berger rhythm potential changes from the occipital lobes in man *Brain* 1934 *57* 355 384

BARTLEY S H Relation of intensity and duration of brief retinal stimulation by light to the electrical response of the optic cortex of the rabbit *Amer J Physiol* 1934 *108* 397 408

BARTLEY S H Some observations on the organization of the retinal response *Amer J Physiol* 1937 *120* 184 189

BERTRAND I GUILLAIN J and MAZARS G La méthode des excitations periphériques en electro encephalographie *Compt Rend Soc Biol* 1945 *139* 24-30

BISHOP G H and O LEARY J Components of the electrical response of the optic cortex of the rabbit *Amer J Physiol* 1936 *117* 292-308

CASE T J Alpha waves in relation to structures involved in vision *Biol Symposia* 1942 *8* 107 116

COBB S Photic driving as a cause of clinical seizures in epileptic patients *Arch Neurol Psychiat* 1947 *58* 70 71

COHN R The occipital alpha rhythm A study of phase variations *J Neurophysiol* 1948 *11* 31-37

CRUIKSHANK R M Human occipital brain potentials as affected by intensity — duration variables of visual stimulation *J Exp Psychol* 1937 *21* 625-641

DAWSON G D Cerebral responses to electrical stimulation of peripheral nerve in man *J Neurol Neurosurg Psychiat* 1947A *10* 137 140

DAWSON G D Investigations on a patient subject to myoclonic seizures after sensory stimulation *J Neurol Neurosurg Psychiat* 1947B *10* 141-162

DAWSON G D and WALTER W GREY The scope and limitations of visual and automatic analysis of the electroencephalogram *J Neurol Neurosurg Psychiat* 1944 *7* 119-133

DELGADO J M R and LIVINGSTON R B Some respiratory vascular and thermal responses to stimulation of orbital surface of frontal lobe *J Neurophysiol* 1948 *11* 39 55

DEMPSEY E W and MORISON R S The electrical activity of a thalamocortical relay system *Amer J Physiol* 1943 *138* 283 296

DROOGLEEVER-FORTUYN J D and JASPER H H Thalamic centres controlling rhythmic electrical activity of the cortex *Proc XVII Internat Physiol Congr* Oxford 1947 368 369

DUBNER H H and GERARD R W Factors controlling brain potentials in the cat *J Neurophysiol* 1939 *2* 142-152

DURUP G and FESSARD A L électro encéphalogramme de l homme Observations psycho physiolo

gique relative a l action des stimuli visuel et auditif *Ann Psychol* 1935 *36* 1-35

FISCHER M H Elektrobiologische erscheinungen au der Hirnrinde bei Belichtung eines Auges II *Arch f d ges Physiol* 1934 *233* 738-753

GASTAUT H ROGER J and GASTAUT Y Les formes experimentales de l epilepsie humaine 1 l Epilepsie induite par la stimulation lumineuse intermittente rythmee ou epilepsie photogenique *Rev Neurologique* 1948 *80* 161-183

GOLDMAN G SEGAL J and SEGALIS M L action d une excitation intermittente sur le rythme de Berger *Compt Rend Soc Biol* 1938 *127* 1217-1220

GOLLA F L HUTTON E L and WALTER W GREY The objective study of mental imagery *J Ment Sci* 1943 *89* 216-223

HALSTEAD W C KNOX G W and WALKER A E Modification of cortical activity by means of intermittent photic stimulation in the monkey *J Neurophysiol* 1942 *5* 349-356

HALSTEAD W C KNOX G W WOOLF J I and WALKER A E Effects of intensity and wave length on driving cortical activity in monkeys *J Neurophysiol* 1942 *5* 483-486

JASPER H H Cortical excitatory state and synchronism in the control of Bioelectric autonomous rhythms *Cold Spring Harbor Symposia on Quantitative Biology* Cold Spring Harbor (L I New York), 1936 *4* 320-338

KNOX G W Investigations of flicker and fusion *J Gen Psychol* 1945 *33* 121-154

KORNMULLER A E Architektonische Lokalisation bioelektrischer Erscheinungen auf der Gross Hirnrinde I Untersuchungen am Kaninchen bei Augenbelichtung *J Psychol u Neurol* 1932 *44* 447-459

KRUGMAN H E Flicker fusion frequency as a function of anxiety reaction an exploratory study *Psychosom Med* 1947 *9* 269 272

LIVANOV M N Les processus des frequences dans l electrocerebrogramme *Bull Biol Med Exp* USSR 1938 *5* 248-251

LIVANOV M N Rhythmic stimulation and the interrelationship of cortical zones *J Physiol* USSR 1940 *28* 172-182

LIVANOV M N and PETROVA N G Analysis of the electrocerebrogram of the visual zone under the action of two simultaneous stimuli *Med Exp* Ukraine 1938 *2* 31-38

LIVANOV M N and POLIAKOV K L Electrical processes in the rabbit s cortex during the development of a conditioned defence reflex in response to rhythmic stimulation *Bull Acad Sci* USSR, 1945 *3* 286-307

LOOMIS A HARVEY N and HOBART G Electrical potentials of the human brain *J Exp Psychol* 1936 *191* 249-271

MARSHALL W H Observations on subcortical somatic sensory mechanisms of cats under nembutal anesthesia *J Neurophysiol* 1941 *4* 25-43

MARSHALL W H TALBOT S A and ADES H W Cortical response of the anesthetized cat to gross photic and electrical afferent stimulation *J Neurophysiol* 1943 *6* 1-15

MARSHALL W H WOOLSEY C N and BARD P Observations on cortical somatic sensory mechanisms of cat and monkey *J Neurophysiol* 1941 *4* 1-24

McCULLOCH W S Modes of functional organization of the cerebral cortex *Fed Proc* 1947 *6* 448-451

MONNIER M Mesure du temps retino-cortical a partir des potentiels evoques par stimulation lumineuse chez l homme *Helv Physiol* Acta 1948, *6* 61-62

MONNIER M L Electro-retinogramme de l homme *EEG Clin Neurophysiol* 1949 *1* 87-108

MORISON R S and DEMPSEY E W Mechanism of thalamocortical augmentation and repetition *Amer J Physiol* 1943 *138* 297-308

PITTS W and McCULLOCH W S How we know universals The perception of auditory and visual forms *Bull Math Biophys* 1947 *9* 127-147

TOMAN J Flicker potentials and the alpha rhythm in man *J Neurophysiol* 1941 *4* 51-61

WALKER A E, WOOLF J I HALSTEAD W C and CASE T J Mechanism of temporal fusion effect of photic stimulation on electrical activity of visual structures *J Neurophysiol* 1943 *6* 213-219

WALKER A E WOOLF J I HALSTEAD W C and CASE T J Photic Driving *Arch Neurol Psychiat* 1944 *52* 117-125

WALTER W GREY Analytical means of studying the nature and origin of epileptic disturbance *Res Publ Ass nerv ment Dis* 1946 *26* 237-251

WALTER W GREY and DOVEY V J Etude analytique des rythmes corticaux induits par une stimulation lumineuse intermittente *Marseille Med* 1947 *5* 240 248

WALTER, W GREY DOVEY V J and SHIPTON H W Analysis of the electrical response of the human cortex to photic stimulation *Nature* 1946 *158* 540-541

WALTER W GREY HILL D and WILLIAMS, D Discussion on the electroencephalogram in organic cerebral disease *Proc Roy Soc Med* 1948 41 237-250

WALTER W GREY and WALTER V J The electrical activity of the brain *Ann Rev Physiol* 1949 (In Press)

WALTER W GREY WALTER V J GASTAUT H and GASTAUT Y Une forme electroencephalographique nouvelle de l epilepsie l epilepsie photogenique 1st French EEG meeting March, 1948

WANG G H Action potentials of the visual cortex and the superior colliculus induced by stimulation of the retina with light *Chinese J Physiol* 1934 *8* 121-144

WARD A A The Cingular Gyrus area 24 *J Neurophysiol* 1948 *11* 13-23

WARD A A and McCULLOCH W S The projection of the frontal lobe on the hypothalamus *J Neurophysiol* 1947 *10* 309-314

WEDDELL G SINCLAIR D C and FEINDEL W H An anatomical basis for alterations in quality of pain sensibility *J Neurophysiol* 1948 *11* 99-109

WOOLF J I WALKER A E KNOX G W, and HALSTEAD W C The effect of lesions of the visual system on photic driving *J Neuropath Exp Neurol*, 1945 *4* 59-61

L'ÉLECTRO RÉTINOGRAMME DE L'HOMME [1]

Marcel MONNIER
Institut de Physiologie de l'Université de Zurich (Suisse)

INTRODUCTION

Il existe entre la surface postérieure et la surface antérieure de la rétine au repos même dans l obscurité une différence de potentiel de quelques millivolts Le courant électrique produit par cette différence de potentiel (potentiel de repos) a l intérieur de la rétine va de l extrémité des récepteurs (cônes et bâtonnets) a leur base en connexion avec les cellules bipolaires les cellules ganglionnaires et leurs fibres Dans le milieu extra-oculaire le même courant passe de la cornée électro-positive a la paroi postérieure du globe oculaire électro-négative On peut le dériver chez tous les animaux et chez l'homme a l'aide d une électrode sur la cornée et d une autre électrode placée le plus près possible de la paroi postérieure du globe oculaire en un point quelconque de l orbite (fig 8) L éclairement de la rétine produit des variations de ce potentiel de repos variations que l on enregistre de façon que toute augmentation de positivité au niveau de la cornée se traduise par une deflexion du tracé au-dessus de la ligne de base On obtient dans ces conditions une courbe polyphasique typique l *électro-rétinogramme* (*ERG*)

Depuis les premières démonstrations de l'activité bio-électrique de la rétine chez l animal les physiologistes ont essayé a maintes reprises de dériver les potentiels rétiniens d éclairement chez l homme Ils se sont heurtés a l origine a des difficultés techniques considérables provenant du sujet d une part des électrodes et du galvanomètre a corde alors en usage d'autre part (Dewar 1877 Kahn et Lowenstein 1924 Hartline 1925 Sachs 1929 Kohlrausch 1931 1932 Cooper Creed et Granit 1933 Groeppel Haass et Kohlrausch 1938)

L utilisation plus récente d'électrodes perfectionnées d'amplificateurs a valves et d oscillographes cathodiques a beaucoup facilité les explorations électro-rétinographiques chez l homme (Bernhard 1940 Karpe 1945 Monnier et Boehm 1945 Monnier 1946) L utilisation d oscillographes a encre (Riggs 1941 Adrian 1944 1945) a également donné de bons résultats

Aujourd hui l électro-rétinographie est sur le point de devenir comme l électro-cardiographie et l électro-encéphalographie une méthode diagnostique clinique permettant de contrôler objectivement les processus de réception de la rétine (Karpe 1945 Monnier et Amsler 1945 Monnier et Jeanneret 1947) Avant de passer a l étude des manifestations électriques pathologiques de la rétine nous avons analysé qualitativement et quantitativement les manifestations électriques de la rétine normale dans diverses conditions d éclairement A cette fin nous avons mis au point avec le précieux concours de notre collaborateur F Boehm une technique adéquate pour la dérivation l amplification et l enregistrement des potentiels rétiniens chez l homme Nous avons perfectionné également notre méthode de stimulation lumineuse afin d étudier successivement l influence de la durée de l intensité et de la qualité du stimulus lumineux (longueur d onde) sur la rétine humaine ainsi que l influence de l endroit de la rétine éclairé Nous avons pratiqué aussi des enregistrements binoculaires et analysé les manifestations électriques consensuelles qui surviennent a l œil contralatéral quand on éclaire l œil ipsilatéral Enfin en combinant l ERG et l EEG nous avons déterminé le temps qui s écoule entre

[1] Travail subventionné par la Fondation Rockefeller et le Fonds de la Recherche scientifique de l Université de Zurich Communication préliminaire au XVIIe Congrès International de Physiologie Oxford Juillet 1947

gique Ann debut des decharges retiniennes et le blocage du rythme α au niveau de l ecorce cerebrale Cette valeur nous renseigne sur le fonctionnement des voies et des centres optiques

TECHNIQUE

Le sujet est assis devant un perimetre sur l arc duquel est monte le dispositif de stimulation lumineuse (fig 1) Ce dispositif mobile se compose de la source lumineuse de diaphragmes lentilles (L) et filtres de couleur (F) Il permet de projeter sur les divers champs de la retine un spot lumineux circonscrit de duree et d intensite reglables de longueur d onde definie Les examens de controle pratiques sur un œil de porc ont montre que l etendue du spot lumineux sur la retine est inferieure a celle que produirait un disque lumineux de 2° dans le champ visuel L œil examine se trouve au centre de l arc du perimetre Il fixe une petite lampe rouge (R) centree sur l axe de cet arc a 30 cm de distance L intensite de cette lampe est reduite au minimum compatible avec une bonne fixation du regard son activite electro retinographique est nulle

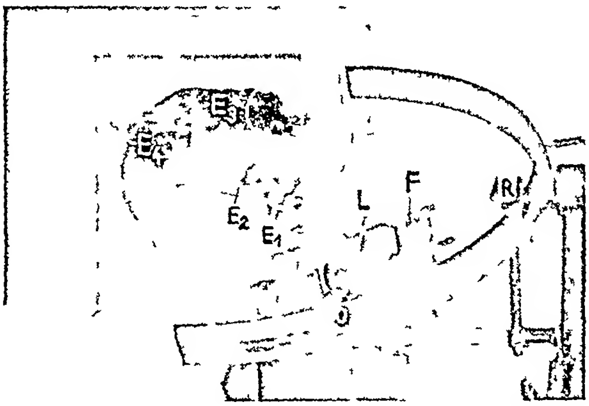


Fig 1

Technique de l electro retinographie perimetrique chez l homme E_1 Electrode corneenne E_2 Electrode temporale E_3 et E_4 Electrodes pour l'enregistrement simultane de l EEG Explication dans le texte

Pour la stimulation lumineuse nous nous sommes servis d une petite ampoule de 6 V/15 W, dont le faisceau concentre a l aide de lentilles et de diaphragmes est interrompu a volonte par un relai ou obturateur electro magnetique (0) La lampe reste allumee pendant toute la duree de l experience *sa constante de temps ne joue aucun role* puisque la duree de la phase d eclairement est conditionnee exclusivement par l ouverture d un volet (shutter), actionne par un petit electro aimant Le jeu de cet obturateur electromagnetique est regle soit par l operateur lui-meme, en-dehors de la cabine blindee soit par un interrupteur automatique (disque rotatoire muni de cames) apte a produire des stimuli lumineux periodiques, de duree definie On obtient en reponse a cette *stimulation intermittente* (flicker) une serie d ERG qui presente l avantage de stabiliser des le 3e ou 4e stimulus les conditions d adaptation pupillaire et retinienne L experience a montre que la periodicite optimum est realisee quand une phase d eclairement d 1/10 de seconde alterne avec une phase d obscurcissement de 9/10 de seconde Les ERG enregistres dans ces conditions presentent des deflexions amples et un minimum de perturbations d origine motrice reactions palpebrales mouvements oculaires

Les *stimuli lumineux isoles prolonges* pendant 2 secondes produisent aussi d excellents ERG Pour avoir des conditions comparables il est indispensable, dans ce cas de definir l etat d adaptation de la retine Un obscurcissement de 3 minutes, si possible avant chaque stimulus permet de realiser facilement des conditions d adaptation retinienne constantes

L intensite du stimulus lumineux est dosee a l aide d un rheostat et d un amperemetre Nous nous sommes limites en general a 3 ou 5 intensites I a V La brillance du spot lumineux sur la retine a ete determinee aussi exactement que possible a l aide d une cellule photoelectrique placee derriere un œil de porc, trepane au niveau de la fovea centralis et eclaire dans les memes conditions que l œil du sujet Ce contrôle a donne une brillance de 0 1 lumen environ au niveau de la retine pour l intensite II

Les potentiels retiniens sont derives a l aide d electrodes impolarisables liquides, du type d Arsonval modifie L une en contact avec la cornee par une meche de coton (E_1) est fixee a la monture d une paire de lunettes selon la technique d Adrian (1945) L autre est collee a la tempe avec du collodion (E_2 Monnier et Amsler 1945) La cornee est convenablement anesthesiee pendant toute la duree de l examen (Larocaine Roche 1%) On obtient par ce mode de derivation des ERG aussi stables que ceux enregistres a l aide d electrodes en verres de contact (Karpe 1945) Si l on stabilise l adaptation pupillaire en utilisant une stimulation lumineuse intermittente la dilatation de la pupille par instillation d atropine devient superflue

Les potentiels ainsi derives sont amplifies environ 2 000 000 de fois a l aide d un amplificateur a 3 etages montage push-pull et couplage galvanique direct Ils sont appliques ensuite aux plaques de deflexion de 2 oscillographes cathodiques, puis enregistres photographiquement (Boehm Sigg et Monnier 1944 Monnier et Boehm 1945)

RÉSULTATS ET DISCUSSION

Caracteres generaux de l'ERG chez l'homme

L'analyse de plus de 1 800 traces, enregistres chez plusieurs sujets normaux selon la technique precedemment decrite, a montre que l ERG de l'homme presente un comportement polyphasique, semblable, dans ses grandes lignes a celui de la plupart des animaux, notamment des vertebres (fig 2 A B = ERG du cobaye, C D = ERG de l'homme)

Un *stimulus lumineux continu* (2 sec fig 2 C) produit apres une periode de latence de 50 a 80 m sec (L) une deflexion negative tres faible et inconstante (potentiel a) suivie d une elevation primaire ample et constante (potentiel b) Ce potentiel b+ composante principale de l ERG atteint son point culminant 50 a 100 m sec apres le debut du stimulus (t c = temps de culmination) il presente une amplitude moyenne de 130 a 300 μV pour les conditions experimentales dans lesquelles nos mesures ont ete faites On admet que le debut du potentiel b coïn-

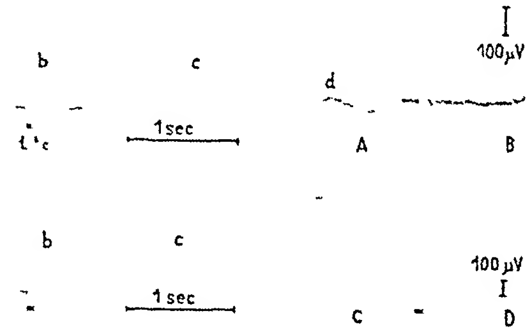


Fig 2

Electro retinogrammes du cobaye (A B) et de l homme (C D) La deflexion initiale negative a manque sur ces traces on la voit par contre sur ceux de la Fig 7 b = elevation primaire positive c = elevation secondaire positive d = potentiel d extinction ou off effect positif en A negatif en C absent en B et D

cide avec le debut des decharges retiniennes dans le nerf optique A la phase d elevation rapide succede une phase decroissante, un peu plus lente qui tend a ramener le trace a la ligne de base et peut l'abaisser même dans certains cas au-dessous de cette derniere Cette negativation, que nous avons appelee potentiel b— paraît avoir souvent une origine extra-retinienne mouvements des globes oculaires, reaction irienne Elle peut être réduite considerablement ou supprimee par l emploi de verres de contact par la dilatation de la pupille (Karpe 1945) mais aussi par l utilisation de stimuli lumineux intermittents et colores (Monnier et Boehm 1947) A la suite de l elevation primaire (potentiel b) il peut se produire une elevation secondaire, lenlans l'etat d adaptation tiel c) On admet quetopique) que dans tant est plus ou moinsçurite (etat scotodegre d excitabilite de la par exemple la tion du stimulus a pour effet eclairs par serapidement et de ramener le trd de 7 seulede depart s il n y etait pas reverit et Ridment deja pendant la periode d'ec Cette suppression du stimulus ne proponses mais de potentiel terminal positif chez l timuli ation me alors que c est la regle chez la plurnt des vertebres (potentiel d potentiel d'es tinction ou off-effect, fig 2A)

Une *stimulation lumineuse intermittente* (periode d eclairement de 0 1 sec, periode d obscurcissement de 0 9 sec, fig 2 B D) produit une serie d'ERG plus simples, en general que ceux declenches par une stimulation lumineuse prolongee La composante principale en est le potentiel b+, le potentiel c apparaît plus rarement dans ces conditions De même, on n'observe pas de deflexion apres la cessation du stimulus puisqu'il n'y a pas d elevation secondaire et pas de deplacement de la ligne de base

Les diverses composantes de l ERG ont ete analysees par Einthoven et Jolly (1908) Piper (1911), Adrian et Matthews (1927) Granit (1932 1933) En etudiant l action selective de divers facteurs physico chimiques sur l ERG de l animal Granit est parvenu a la conclusion que l ERG des mammiferes est la resultante de 3 composantes et processus distincts les processus PI PII et PIII dont l ordre chronologique correspond a celui de leur disparition sous l influence d une narcose progressive a l ether Le processus PI qui disparait le premier et correspond dans ses grandes lignes au potentiel c ne produit aucune decharge dans le nerf optique Le processus PII est essentiellement responsable du potentiel b et se traduit par une decharge d influx dans le nerf optique il est affecte par le manque d oxygene et intensifie par l alcool Quant au processus PIII c est un processus inhibiteur qui tend a negativer l ERG au debut de la stimulation lumineuse (potentiel a) Il est plus prononce pendant l adaptation a la lumiere et quand le stimulus augmente d intensite ou de durée Sa cessation au moment de l extinction du stimulus lumineux se traduit par une decharge d influx dans le nerf optique veritable rebound responsable du potentiel d extinction off-effect ou potentiel d Ce processus inhibiteur serait aboli facilement par l alcool

Granit (1947) a insiste sur le fait que le developpement des diverses composantes de l ERG varie considerablement suivant les conditions d adaptation de la retine L analyse exacte de ces variations lui a permis de distinguer deux types de retine caracterisés par une structure et des fonctions differentes le type E (excitatory type) et le type I (inhibitory type)

giquc pour systeme recepteur
Anrdebut des dechargese essentiellement de bâ-
Blocage du rythme αerce surtout des fonctions
cerebrale Cette va capter les stimuli lumineux
le fonctionnemerapte a l obscurite (etat scoto-
optiques est particulierement frequent chez
on le trouve a l etat presque pur
omme le montrent les traces a et b de
im Sigg et Monnier 1944) Du point
Le sujet ectrique les retines du type E se carac-
duquel est des modifications plus prononcees au
neuse (f l eclairement qu apres l extinction quand la
source t adaptee a la lumiere (etat photopique) Le
filtres iel terminal d (off-effect) est faible et lent Si
div applique au moment ou il se manifeste un nou-
cc au stimulus lumineux il se produit un potentiel b
subnormal que ne precede aucune encoche negative
c est-a-dire aucun potentiel a

Les retines du *type I* ont pour systeme recepteur dominant un appareil compose essentiellement de cônes *Elles exercent surtout des fonctions* de differenciation et signalent dans l œil adapte a la lumiere (etat photopique) les changements qui surviennent dans le champ visuel variations d eclairement deplacements du lieu de la retine eclairee differences de couleur Le type I est particulierement developpe chez les animaux a sang froid (poissons, amphibiens, reptiles) et chez les oiseaux on le trouve a l etat presque pur chez la tortue et le serpent L exploration electro-retinographique montre que les modifications de l ERG sont plus prononcees au moment de l extinction du stimulus lumineux qu a son debut quand la retine est adaptee a la lumiere (etat photopique) Le potentiel initial a est net mais c est surtout le potentiel terminal d (off-effect) qui frappe par son developpement et sa positivite au moment de l extinction Si l on applique immediatement apres l extinction un nouveau stimulus lumineux il provoque un potentiel a super normal

Le developpement extrêmement faible du potentiel negatif initial (potentiel a) et l absence de deflexion terminale positive (potentiel d) permettent d assimiler l'ERG humain au type E de Granit Le nombre des elements sensibles a l extinction (cônes) est apparemment trop faible pour produire un potentiel terminal prononce Par contre, le potentiel b+ engendre essentiellement par les bâtonnets comme l'ont demontre Adrian (1945) et Karpe (1945) est tres prononce dans l'ERG de l'homme

L'electro-retinographie binoculaire et la reponse electrique consensuelle

Nous avons explore simultanement le comportement electrique des 2 yeux en reponse a l eclairement d une seule retine A cette fin il etait indispensable d isoler les 2 yeux, a l aide d un ecran fixe sur la ligne mediane du front et du nez Dans ces conditions l œil gauche ne recevait aucune lumiere quand dans l obscurite on eclairait isolement l œil droit Les manifestations electriques de chaque œil etaient derivees, comme d habitude au moyen de 2 electrodes l une en contact avec la cornee l autre fixee a la tempe L experience est repetee apres dilatation de la pupille droite (Homatropine) elle se termine par un enregistrement simultane des reponses electriques des 2 yeux a l eclairement de l œil gauche non dilate (Monnier 1946b)

Fig 3

Electro-retinographie binoculaire ERG normal a l œil droit (O d) en reponse a l eclairement du même œil Reponse consensuelle d origine irienne probable a l œil gauche (O g)

De ces experiences, il ressort que l eclairement d une seule retine la droite produit un ERG typique a l œil droit eclaire (potentiels b et c) ainsi qu'une reponse consensuelle a l œil gauche non stimule (fig 3) Ce phenomene avait ete constate chez l animal deja par Grijns (1891) La reponse consensuelle debute 300 a 320 m sec et atteint son maximum 600 m sec apres le debut du stimulus Elle est caracterisee par une elevation à peine plus faible que celle du potentiel c et evolue parallelement au potentiel c de l'œil eclaire, mais avec une legere difference de phase Elle debute en effet quelques m sec apres le potentiel c de l'œil eclaire et atteint son point culminant quelques m sec apres le sien Pendant la periode d elevation, la pente des 2 courbes est assez abrupte et parallele Le retour a la ligne de base s effectue, par contre en pente plus douce souvent plus rapidement sur le trace consensuel que sur celui de l œil eclaire

Si l'on paralyse l iris de l'œil droit par une instillation d'atropine et que l on eclaire l'œil gauche on n observe plus de manifestation consensuelle nette a l œil droit atropinise Cette observation semble indiquer que la reponse consensuelle n'est peut-être que la manifestation electrique du reflexe photomoteur consensuel (electro-iridogramme) Pour preciser ce point nous avons filme avec W Koella les reactions pupillaires provoquees

par la stimulation lumineuse intermittente que nous utilisons habituellement en electro-retinographie Nous avons enregistre ensuite l'ERG chez le même sujet afin de comparer les temps de reaction de la retine et de la pupille (Monnier 1947) Ces examens de contrôle ont montre que la constriction pupillaire debute 230 a 300 m sec apres le debut du stimulus et qu elle atteint son maximum en 300 a 450 m sec (temps de culmination de la constriction pupillaire)

Il y a donc correspondance entre les temps de latence et de culmination du potentiel c a l œil eclaire les temps de l effet consensuel et ceux de la constriction pupillaire Nos chiffres correspondent a ceux de Van Brunn Falk Matthes et Matthes (1941) et a ceux de Tschirren (1947) qui ont mesure un temps de latence de 260 a 300 m sec et un temps de constriction pupillaire de 500 a 550 m sec comptes depuis le debut jusqu au maximum de la constriction Le temps de latence du reflexe palpebral n est par contre que de 70 m sec Ces faits nous indiquent que la prudence est de riqueur quand on interprete le potentiel c d un œil non dilate et l effet consensuel analogue obtenus par l'electro-retinographie binoculaire Ces 2 phenomenes en effet se manifestent en même temps que le reflexe pupillaire photomoteur direct et consensuel

Influence de l'adaptation et de la duree du stimulus lumineux sur l'ERG (Discrimination de la frequence des stimuli intermittents)

La stimulation lumineuse intermittente permet d examiner dans quelle mesure la retine est capable d analyser les changements rapides d eclairage L exploration bio-electrique montre que la retine repond aux stimuli intermittents par une succession de petits potentiels b nettement individualises quand la frequence des stimuli n est pas trop elevee

Le pouvoir de discrimination de la retine a l egard des changements brusques d eclairement peut être exprime par la *frequence de fusion* Celle-ci varie suivant l etat d adaptation quand il s agit de rétines mixtes Elle est plus elevee dans l'etat d adaptation a la lumiere (etat photopique), que dans l etat d adaptation a l obscurite (etat scotopique) Chez la grenouille par exemple, la frequence de fusion est de 13 eclairs par seconde dans l etat photopique et de 7 seulement dans l etat scotopique (Granit et Riddell 1934)

Granit (1947) a precise le caractere des reponses electriques de la rétine et du nerf optique aux stimuli lumineux intermittents dans les états d adaptation photopique et scotopique Le caractere tres different des ripostes enregistrees dans ces diverses conditions a constitue un critere de plus pour la distinction des 2 types de retine E et I

Une rétine du *type E* (excitatory type) repond a une stimulation intermittente par la production de potentiels b subnormaux dans l ERG et d une volee d influx excitateurs dans le nerf optique La periode de latence de ces potentiels b parait souvent allongee signe que l on peut mettre en parallèle avec le developpement du potentiel a dans les rétines du type I (Creed et Granit 1933) Quant a la frequence de fusion des excitations produites par la stimulation intermittente elle est basse meme quand la retine est adaptee a la lumiere

Une retine du *type I* (inhibitory type) repond a une stimulation intermittente rapide par une succession de potentiels a tres nets au debut de chaque stimulus et de potentiels d positifs a l extinction La frequence de fusion des reponses a une stimulation intermittente est elevée dans l etat photopique Cette propriete de discrimination peut etre attribuee au potentiel a de l ERG et a la volee d influx (preexcitateurs) inhibiteurs qui lui correspondent dans le nerf optique Ceux ci ont pour effet d interrompre le rebound de l excitation au moment de l extinction Cette inhibition preexcitatrice parait etre une des contributions essentielles du systeme des cones a la vision elle est peut etre liee a l existence de cellules amacrines (Granit) L aptitude des retines du type I a repondre aux changements rapides d eclairage implique donc l alternance d un processus inhibiteur preexcitateur (processus III manifeste par le potentiel a) et d un processus excitateur (processus II manifeste par le potentiel b)

De ces diverses donnees experimentales nous retiendrons surtout que pour la retine du type E la frequence de fusion des excitations provoquees par une stimulation intermittente est relativement basse même pendant l adaptation photopique Or c'est precisement le cas aussi pour la retine humaine, assimilable nous l avons dit au type E

Chez l homme on avait examine autrefois deja par les methodes subjectives l influence de l adaptation retinienne sur le seuil de la sensation de scintillement (flicker) Ainsi Schaternikov (1902) avait etabli que l adap-

tation a la lumiere a pour effet d elever la frequence de fusion (jusqu'a 30 par seconde) Par la suite on a constate en outre que l'elevation de la frequence de fusion provoquee par l'adaptation a la lumiere est plus prononcee pour la retine peripherique composee de bâtonnets et de cônes que pour la retine centrale composee uniquement de cônes

Ces donnees ont ete contrôlees objectivement depuis par l'electro-retinographie En 1929, Sachs a constate qu'une stimulation intermittente de 5 a 10 eclairs par seconde produit subjectivement une sensation du scintillement grossier et objectivement une succession de potentiels tres nets sur l'ERG Quand la frequence des stimuli depasse celle qui produit le seuil de fusion subjective l examen electro-retinographique révele aussi une fusion des excitations retiniennes Il existerait donc, selon Sachs, une concordance entre les seuils de fusion subjectif et objectif, Copper Creed et Granit (1933) ont enregistre chez l'homme egalement, une succession de potentiels retiniens en reponse a une stimulation lumineuse intermittente de basse frequence, (8 p sec) La faible amplitude des oscillations et l instabilite de la ligne de base n'ont pas permis a ces auteurs de prouver l'existence d une correlation etroite entre la fréquence de fusion subjective et celle determinee par l'ERG Bernhard (1940) a confirme que la stimulation intermittente produit chez l homme un potentiel b initial d'amplitude normale, suivi d une serie de potentiels b moins amples Ces oscillations disparaissent quand la frequence depasse 20 stimuli par seconde, par contre la sensation de scintillement ne disparaît dans ces experiences que lorsque les stimuli ont une frequence de 25 a 26 par seconde

Observations personnelles Pour contrôler la frequence de fusion normale chez l homme nous avons entrepris une serie d experiences a l aide d un stimulateur specialement construit a cette fin La stimulation intermittente utilisee par la plupart des expérimentateurs se caracterise par une alternance de phases d eclairement et d obscurcissement Ces phases sont généralement dans un rapport constant l une par rapport a l autre mais leur duree absolue varie en fonction de la frequence utilisee Ainsi quand la frequence des stimuli augmente, la duree de chaque phase diminue Pour eviter l inconvenient des variations de duree de la phase d eclairement nous nous sommes servis d un interrupteur mecanique permettant de produire des eclairs de duree constante (1/75 sec environ) quelle que soit la frequence choisie La phase d obscurcissement présente par contre des variations appreciables de duree en fonction des changements de frequence Notre technique de stimulation differe en outre de celle des autres experimentateurs par le fait que la retine est eclairee directement, à l aide d un faisceau bien focalise et non pas indirectement a l aide d un faisceau lumineux projete sur un ecran reflecteur De plus nous avons veille dans nos experiences a ce que l adaptation soit bien definie c est pourquoi chaque serie de stimuli intermittents etait precedee d une periode d obscurcissement ou d eclairement d une minute Le tableau I resume les resultats de nos mesures du seuil de fusion chez un sujet normal au cours de 3 seances differentes

Tableau I — Determination de la frequence de fusion chez un sujet normal

Date	Adaptation 60 sec	Frequence des stimuli lumineux par sec																
		2	4	6	8	10	12	14	15	16	17	18	19	20	24	26	40	52
16 2 45	Obscurite	+	+	+	+	+			+					+	•	∼	–	–
		+	+			+	•		+		•			+		∼	–	
19 2 45	Obscurite		+	+	+	+	+	+	•	+		+	+	∼		•		•
21 2 45	Obscurite					+	•	+	•	+	+	•	–	–	–	•	•	•
	Lumiere			•		+	+	+		+	+		+	–	–			•

Legende ∼ = Oscillations minimes du trace perceptibles mais non mesurables

Du tableau I il ressort que la retine d'un sujet normal produit encore des reponses individualisees quand la stimulation intermittente a une frequence de 19 a 20 eclairs par seconde La frequence de fusion objective est donc superieure a ces valeurs Dans 2 cas même l ERG presentait encore de petites oscillations nettes mais non mesurables a la frequence 26 Cette valeur correspond au seuil subjectif determine par Bernhard (1940) Chez le sujet que nous avons donne en exemple il y avait parfois concordance entre le seuil de fusion objective et celui de la sensation de fusion Le plus souvent toutefois le sujet percevait encore le scintillement a des frequences superieures a celles du seuil objectif On peut donc admettre que dans les conditions de notre stimulation intermittente la limite superieure du pouvoir de discrimination peut être legerement superieure a 26 comme en temoigne l experience subjective et sur certains de nos traces l oscillation minime encore decelable a la frequence 26 La periode d adaptation a l obscurite ou a la lumiere qui dans nos experiences precedait le debut d une serie de stimuli etait trop breve pour influencer sensiblement le seuil de fusion

La figure 4 reproduit les traces d une experience de determination du seuil de fusion chez un sujet normal apres adaptation d une minute a l obscurite La stimulation intermittente a basse frequence (2 4, 6 et 8) produit une succession de potentiels b amples et distincts On remarque même aux frequences basses (2 4 et 10) un certain parallelisme entre le rythme des reponses de l ERG et celui de l EEG Si l on augmente la frequence des stimuli (16) on obtient encore une succession de potentiels b individualises mais d amplitude de plus en plus faible La correspondance entre le rythme de l ERG et celui de l EEG a disparu Quand la stimulation atteint la frequence 19 l ERG

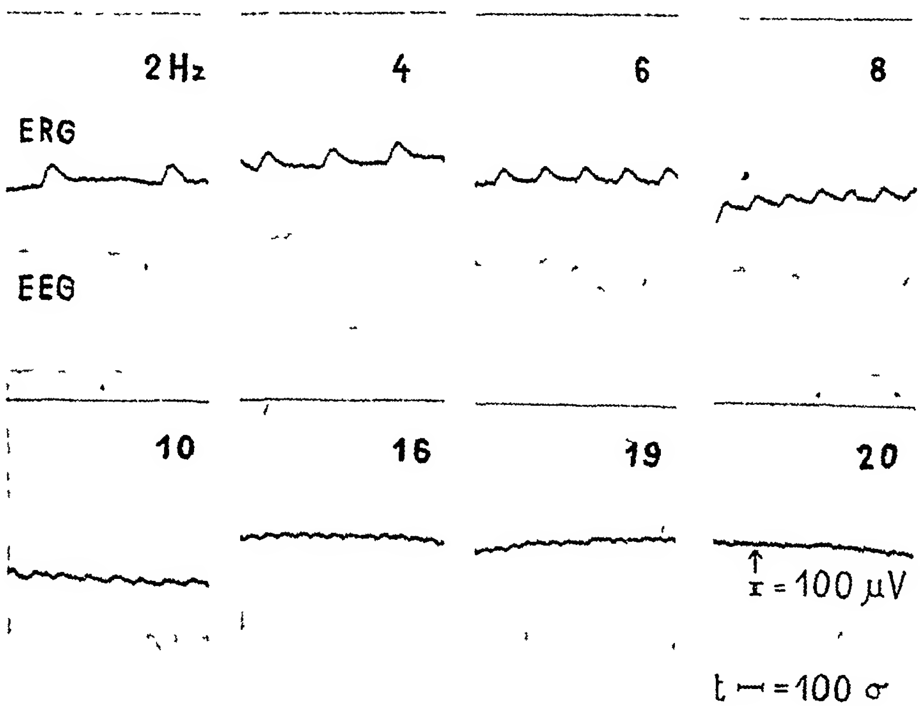


Fig 4
Determination objective de la frequence de fusion Stimulation intermittente de frequence croissante 2 4 6 8 10 16 19 20 eclairs par seconde Fusion complete a la frequence 20

se reduit a une ligne aux oscillations à peine perceptibles celles-ci disparaissent enfin quand la frequence comporte 20 eclairs par sec la fusion objective est alors realisee

La stimulation lumineuse intermittente a pour effet de reduire apres le 1er stimulus deja l'amplitude du potentiel b, c est-a-dire la composante scotopique de l ERG (Adrian 1945) Cette reduction ne se manifeste toutefois qu au debut de la stimulation, elle est probablement due au fait que la retine s est adaptee a la lumiere sous l'influence du 1er stimulus de la serie Nos experiences habituelles realisees a une frequence d un eclair par seconde confirment les observations d'Adrian (tableau II)

W Koella Le reflexe pupillaire est tres ample apres les 2 premiers stimuli, par la suite son amplitude se reduit d ⅓ du fait que la pupille adaptee a un eclairage moyen reste partiellement retrecie Nous considerons cette adaptation moyenne de la retine et de la pupille, realisee par la stimulation lumineuse intermittente (1 c/sec) comme une condition optimum pour l'obtention d ERG stables

Influence de l'intensite du stimulus lumineux sur l'ERG

Toute augmentation de l'intensite du stimulus lumineux a pour effet d'accroître l'amplitude des diverses phases de l'ERG et de

Tableau II — Variations de l'amplitude du potentiel b au cours d'une stimulation lumineuse intermittente (1c/sec)

Sujet	*Intensité du stimulus lumineux*	*Incidence du faisc Retine nas*	Ordre de succession des ERG (Ampl pot b)									
			1	2	3	4	5	6	7	8	9	10
K A	II	60°	200	150	165	150	140	160	150	160	160	140
		20°	300	255	255	225	285	240	240	255	240	255
Ba	II	60°	440	270	220	220	—	220	210	—	—	200
		20°	—	—	380	370	320	280	290	300	310	280
Dr M	III	40°	210	165	175	175	175	150	190	185	—	—
		20°	200	160	150	160	150	160	—	—	—	—
H I	I	40°	100	90	80	90	80	80	80	90	80	80
	II		325	210	310	320	310	310	300	290	280	290
	IV		400	390	400	390	390	—	390	400	390	390
Dr M	I	20°	100	90	90	70	80	85	85	70	80	80
	II		220	185	180	185	200	165	170	180	200	190
	III		285	255	255	265	250	250	250	245	250	255

Du tableau II il ressort que la reduction d'amplitude du potentiel b se manifeste surtout sur le 2e ERG de la serie et parfois encore sur le 3e Les ERG ulterieurs presentent par contre des potentiels b d'amplitude moyenne et relativement peu variable, ce phenomene signifie que l'adaptation retinienne s est stabilisee a un niveau intermediaire entre l etat scotopique et l etat photopique Il en va de même de l'adaptation pupillaire comme l ont prouve nos experiences de contrôle cinematographique avec raccourcir les temps de latence et de culmination du potentiel b (fig 5) Quand cette intensite atteint un certain degre, on peut voir se developper aussi les potentiels negatifs notamment le potentiel a il est peu prononce sur l ERG humain surtout quand le stimulus lumineux n est pas focalise sur la region centrale

Il existe une relation quantitative entre la valeur energetique du stimulus lumineux et l ERG Quand le stimulus est de breve duree et la surface eclairee de faible etendue l effet photoelectrique retinien reste constant meme si l intensite et la duree du stimulus

varient ce n est le cas toutefois que si le produit de ces deux facteurs variables c est-a dire la quantite de lumiere ou d energie lumineuse reste constant Dans ces conditions c est la quantité de lumiere qui conditionne a la fois la vitesse et l amplitude de l effet photoelectrique retinien Cette loi dite *loi de la quantité d energie du stimulus* n est plus valable toutefois quand la durée et l etendue du stimulus lumineux (surface eclairee) dépassent certaines limites La duree superieure pour laquelle la loi est encore valable est de 1/8 sec chez l homme valeur determinée par les methodes subjectives (von Kries 1907) Quant a la limite superieure de la surface eclairee pour laquelle la loi de la quantite d énergie du stimulus est encore valable elle est plus difficile a determiner de façon exacte du fait que sous l influence des phenomenes d aberration toute augmentation de la surface eclairee va de pair avec une augmentation de l intensite du stimulus lumineux La determination du seuil de la sensibilite a la lumiere par les methodes subjectives montre que meme dans les etats d adaptation photopique le seuil ne varie plus en fonction de la surface eclairee mais uniquement en fonction de l intensite du stimulus des que la surface eclairee devient superieure a 10°

site du stimulus lumineux elle est proportionnelle a la racine carree du stimulus Par contre dans la region des *intensites fortes* accrues jusqu'a la provocation des reactions d eblouissement l'amplitude du potentiel b est proportionnelle au logarithme de l intensite du stimulus lumineux (loi de Fechner, confirmee objectivement pour la retine par McKendrick Waller et Haass)

Karpe (1945) a examine l influence des variations d intensite sur l'ERG de l'homme Il a augmente l intensite du stimulus en accroissant progressivement la surface eclairee et constate que l'amplitude du potentiel b augmentait dans un cas proportionnellement au log I mais dans d autres cas qu elle cessait d augmenter deja quand l intensite du stimulus atteignait 5 et 20 lux Il a confirmé,

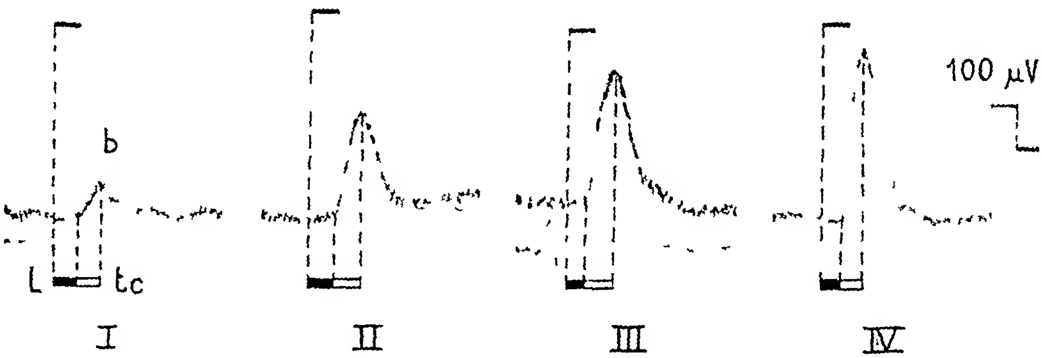


Fig 5

Influence de l intensite du stimulus lumineux sur l potentiel b L augmentation progressive de l intensite (1 2 3 4) raccourcit les temps de latence (L) et de culmination (t c) du potentiel b elle accroit son amplitude La localisation du spot lumineux a la peripherie du champ retinien nasal (40°) explique l absence du potentiel a

La relation entre l intensite du stimulus et l intensite des manifestations electriques retiniennes a ete contrôlee objectivement a maintes reprises chez l'homme (Hartline 1925) et chez l animal (Dewar et McKendrick 1873 Haass 1903 Waller 1905 Chaffee Bovie et Hampson 1923 Chaffee et Hampson 1924 Granit 1932) Les mesures ont montre qu il ne s agit pas d une simple proportion directe mais qu il y a lieu de considerer l'ordre d intensite du stimulus lumineux Pour les *intensites faibles* liminales et supra-liminales l amplitude du potentiel b croît beaucoup plus lentement que l inten-

par ailleurs que l augmentation d intensite du stimulus a pour effet d'augmenter non seulement l'amplitude du potentiel b mais aussi celle du potentiel a en même temps qu elle raccourcit la periode de latence et la McKendrick Waller et Haass)

Observations personnelles Nous avons egalement contrôle l influence de l intensite du stimulus lumineux sur l ERG et nous sommes servis a cette fin de 5 intensites progressives I intensite faible II intensite moyenne egale a 0 1 lumen au niveau de la retine III IV V intensites fortes

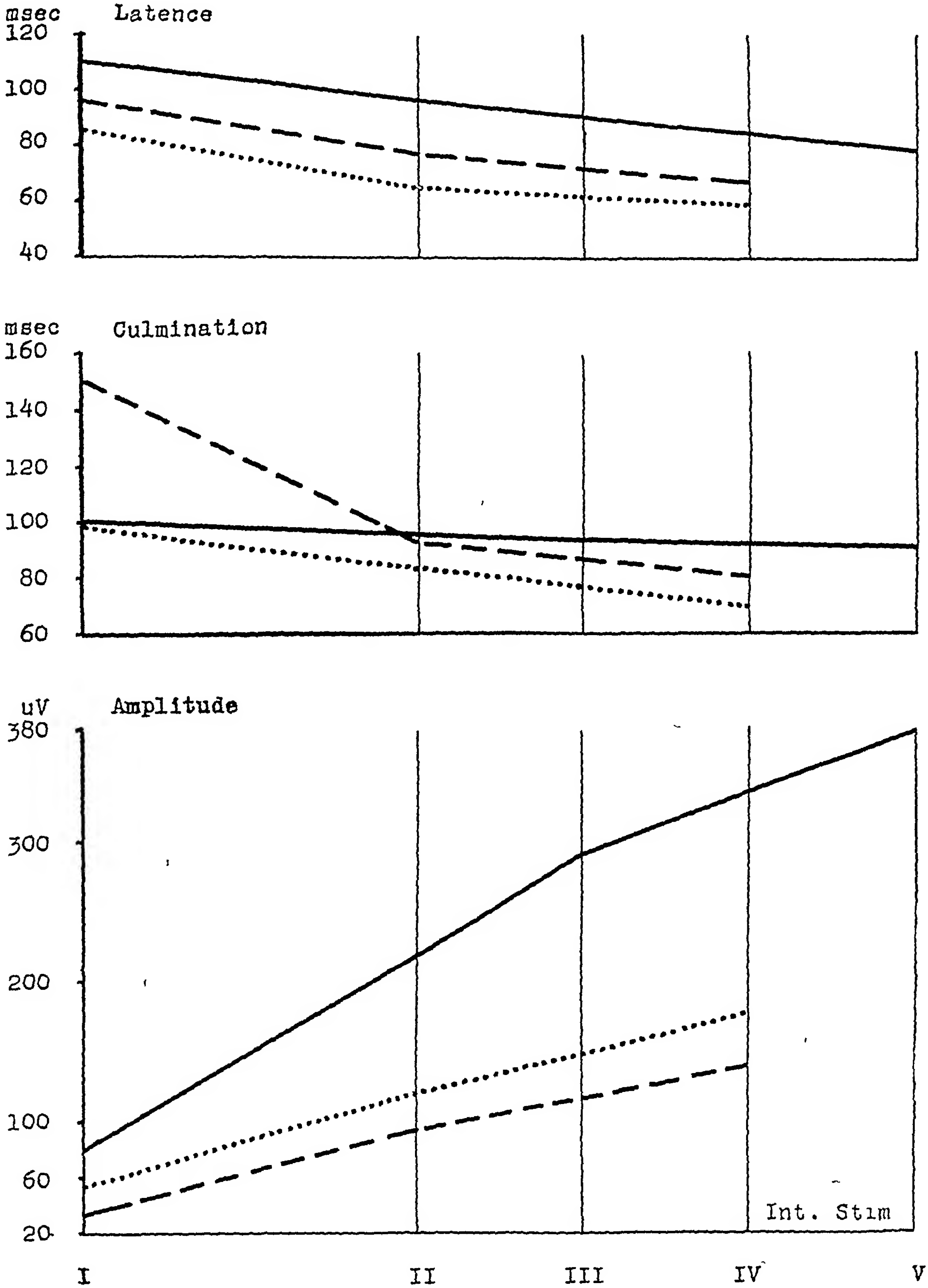


Fig 6

Diagramme des variations du temps de latence du temps de culmination et de l amplitude du potentiel b sous l'influence de l intensite du stimulus 3 sujets normaux

Nos observations ont confirmé que l'augmentation d'intensité du stimulus lumineux a pour effet de raccourcir, d'une part le temps de latence et le temps de culmination du potentiel b et d'augmenter d'autre part l'amplitude de ce potentiel (fig 5) Le raccourcissement du temps de culmination se traduit par une pente plus raide au cours de la phase ascendante du potentiel b L'amplitude du potentiel b peut augmenter de 75% et plus quand l'intensité du stimulus croît du 1er au 3e degré L'amplitude du potentiel a peut augmenter également, elle ne se manifeste pas toutefois sur les tracés de la fig 5 parce que dans l'expérience en question le faisceau lumineux éclairait la région périphérique de la rétine pauvre en cônes (incidence 40°)

Les diagrammes de la fig 6 donnent un aperçu des modifications quantitatives produites par les changements d'intensité du stimulus sur le temps de latence le temps de culmination et l'amplitude du potentiel b

Influence du lieu d'illumination de la rétine sur l'ERG

Il est important de déterminer en vue des applications cliniques éventuelles si l'ERG varie en fonction du lieu de stimulation sur la rétine Cooper Creed et Granit (1933) ont comparé chez l'homme et l'animal les ERG provoqués par l'éclairement d'un champ périphérique de la rétine (30°) à ceux qu'on obtient en stimulant la région centrale Ils ont constaté que l'éclairement de la région centrale produit des potentiels b de 5 à 20% plus amples que ceux qui résultent de la stimulation d'un territoire plus périphérique

L'influence de la localisation du stimulus lumineux sur l'ERG s'est imposée à notre attention au cours de nos premières expériences électro-rétinographiques déjà (Monnier et Amsler 1945) L'analyse de 400 tracés chez le sujet normal a prouvé que l'amplitude du potentiel b augmente de 22 à 42% quand le spot lumineux passe de la périphérie (60°) à une région plus centrale de la rétine (Monnier 1946a) Nos observations récentes sur un nombre encore plus grand de sujets normaux (1 000 ERG) ont montré que non seulement l'amplitude, mais aussi le temps de latence et le temps de culmination du potentiel b varient suivant le lieu illuminé (fig 7) Quand le spot lumineux passe de 60 à 20°, l'amplitude du potentiel b augmente de 5 à 86%, donc plus encore que dans les expériences de Cooper Creed et Granit (65 à 20%) cependant que le temps de latence diminue de 1 à 15% et le temps de culmination de 1 à 36% (Monnier et Boehm 1947) Quant au potentiel a il apparaît de plus en plus nettement au fur

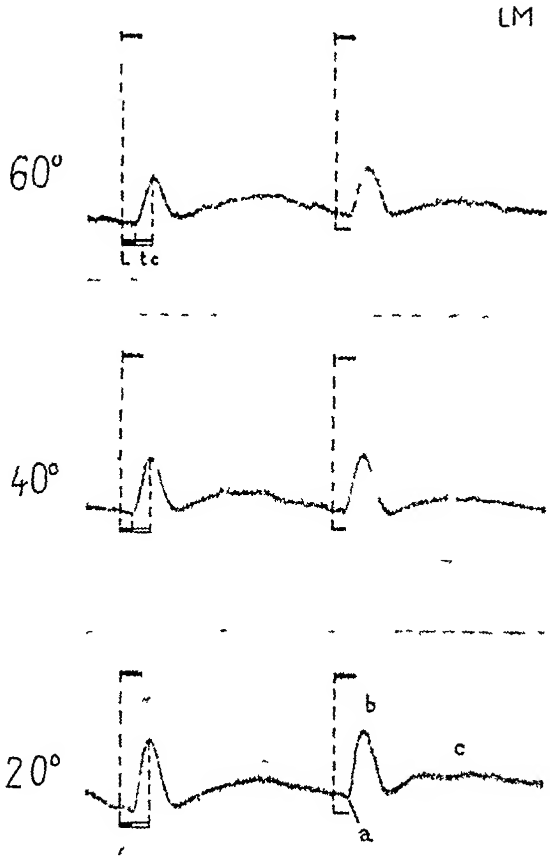


Fig 7

Influence du lieu d'illumination de la rétine sur l'ERG Champ rétinien nasal L'amplitude du potentiel b augmente quand le spot lumineux se déplace de 60 à 20° L = latence b t c = temps de culmination a = potentiel initial plus net quand le spot lumineux se rapproche du centre

et à mesure que l'on excite des regions plus centrales de la retine. Etant donne que ces regions sont plus riches en cônes, on peut en deduire que le developpement du potentiel a est lie a l'activite de ces recepteurs.

Le tableau III donne confirmation de ce fait chez 6 sujets normaux (456 ERG). Dans les exemples cites la moyenne des amplitudes des potentiels b augmente de 30 a 85% de la valeur initiale quand l'incidence du faisceau lumineux passe de 60 à 20° sur le meridien horizontal de la retine nasale. Il est indispensable de connaître le rapport de ces variations d'amplitude en fonction des variations de l'angle d'incidence du faisceau et l'ecart moyen (standard deviation) quand on se propose d'utiliser l'electro-retinographie perimetrique a des fins diagnostiques de 60 a 20° peut determiner a elle seule une augmentation de la quantite de lumiere de 47%.

Le mode de derivation peut egalement conditionner les valeurs quantitatives de la reponse. On sait, en effet, par les experiences sur l'œil excise que le potentiel b diminue d'amplitude quand l'electrode en contact avec la paroi posterieure de l'œil s'eloigne de l'endroit stimule. On peut admettre de même que, dans les conditions de nos experiences la repartition physique des potentiels retiniens en dehors du globe oculaire conditionne la reponse electro-retinographique. Puisque les potentiels retiniens de l'œil droit par exemple sont derives du bord inferieur de la cornee d'une part et de la tempe droite d'autre part on peut

Tableau III. — Influence du lieu d'illumination de la retine sur l'amplitude du potentiel b chez 6 sujets normaux

Incidence du faisceau lumin	*Moyenne des amplitudes des potentiels b*					
	1	2	3	4	5	6
60°	150 ±20	155 ±10	140 ±15	125 ±20	100 ±25	95 ±10
40°		165 ±15	175 ±25	175 ±10	135 ±15	95 ±10
20°	285 ±35	225 ±10	180 ±25	180 ± 5	175 ±10	165 ±35
% Augmentation Totale	85%	45%	30%	45%	75%	75%

Les modifications de l'ERG en fonction du lieu de stimulation de la retine peuvent avoir plusieurs causes. Il y a lieu de considerer tout d'abord le rôle du diaphragme irien qui, suivant l'incidence du faisceau lumineux, peut modifier la quantite de lumiere penetrant vers la retine (fig. 8). Étant donne que cette quantite varie en fonction du cosinus de l'angle compris entre l'axe passant par le point de fixation et le rayon lumineux, une variation d'incidence de ce rayon tres bien concevoir que l'eclairement d'une region peripherique du champ nasal de la retine se traduise par un potentiel b plus faible que celui provoque par une stimulation de la region centrale ou du champ temporal dans ces deux derniers cas le lieu de la retine stimule est plus proche en effet de l'electrode temporale (fig. 8). Or on constate precisement une legere augmentation d'amplitude du potentiel b (jusqu'a 12%) quand le spot lumineux se deplace du centre vers

la périphérie dans le champ temporal de la rétine du côté droit (Monnier et Boehm 1947).

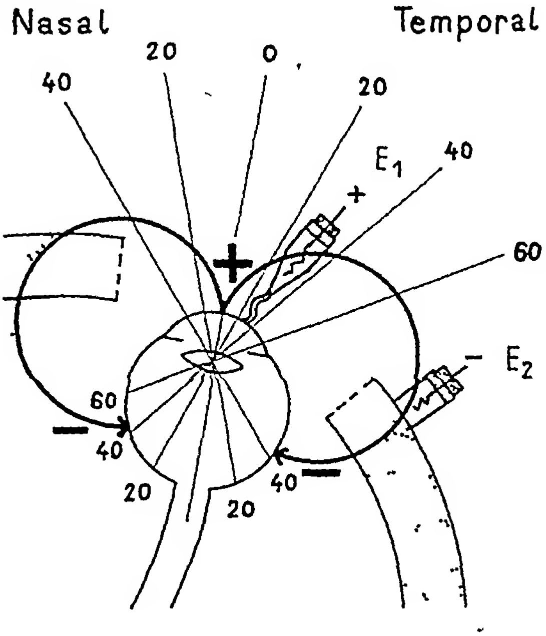


Fig. 8

Distribution des potentiels rétiniens entre la cornée électro-positive et le fond de l'œil électro-négatif. La stimulation de la périphérie du champ rétinien nasal produit des potentiels b de faible amplitude du fait que la distance entre le lieu illuminé et l'électrode temporale E_2 augmente. E_1 = électrode cornéenne. 20° 40° 60° = angles d'incidence du faisceau lumineux avec l'axe de fixation.

Les variations de l'ERG en fonction de l'endroit stimulé ont été attribuées également à une production d'énergie photo-électrique différente suivant la nature et la répartition des éléments rétiniens excités. Cooper, Creed et Granit (1933) ont relevé le fait que dans les régions périphériques de la rétine il existe beaucoup moins de cellules bipolaires et ganglionnaires par rapport aux récepteurs que dans la région centrale. Ces auteurs se sont demandé si la réponse électrique plus faible que l'on obtient en éclairant les territoires périphériques de la rétine n'ont pas un rapport avec le nombre plus petit de cellules bipolaires et ganglionnaires dans cette région. Notre documentation ne nous permet pas de prendre position sur ce point.

Enfin signalons qu'un faisceau lumineux même très bien focalisé comme celui de notre stimulateur exerce, en plus de son action locale à l'endroit du spot lumineux, une certaine action plus faible sur les éléments voisins. Cette action à distance peut être due soit aux connexions nerveuses qui relient les territoires voisins de la rétine, soit à la dispersion des rayons lumineux au cours de leur trajet à travers les milieux optiques. Elle explique de toutes façons pourquoi dans les cas de destruction circonscrite de la rétine, l'éclairement du territoire aveugle à l'examen périmétrique subjectif, produit tout de même une réponse électro-rétinographique. La réponse est toutefois nettement plus faible que celle qui se manifeste quand on éclaire les parties intactes de la rétine (Monnier et Jeanneret 1947).

Lorsque tous les facteurs extra-rétiniens susceptibles d'influencer l'ERG sont pris en considération, comme nous nous sommes efforcés de le faire, notre *méthode d'électro-rétinographie périmétrique* peut être d'une utilité réelle pour le contrôle objectif du champ visuel en ophtalmologie.

Influence de la couleur du stimulus lumineux sur l'ERG

Pour préciser l'influence de la couleur du stimulus lumineux sur l'ERG, il est indispensable d'utiliser des stimuli monochromatiques de valeur énergétique bien déterminée. Par ailleurs il est nécessaire de définir l'état d'adaptation de la rétine et de connaître la répartition de ses éléments — cônes, bâtonnets — dans le champ stimulé. Quand ces conditions primordiales sont définies, l'électro-rétinographie est en mesure d'apporter une contribution importante au problème de la vision des couleurs.

L'électro-rétinographie a permis tout d'abord de contrôler objectivement le *phénomène de Purkinje*. Rappelons que ce phénomène est caractérisé par le fait que la région la plus lumineuse du spectre aux yeux du sujet se déplace du jaune au vert, c'est-à-dire des longueurs d'onde longues aux longueurs d'onde plus brèves, quand la rétine s'adapte à l'obscurité. Quantitativement, on peut exprimer la loi de Purkinje par la *courbe de la sensation de luminosité ou de brillance*; on l'obtient en reportant sur l'axe des abscisses les longueurs d'onde et sur l'axe des ordonnées,

la valeur réciproque de la quantité d'énergie nécessaire pour produire une sensation constante. Si l'on compare alors la courbe de luminosité d'une rétine adaptée à l'obscurité (état scotopique avec activité prédominante des bâtonnets) à celle d'une rétine adaptée à la lumière (état photopique avec activité prédominate des cônes), on constate que pour un spectre d'énergie égale la courbe de la rétine photopique atteint son maximum dans le vert-jaune (longueur d'onde 0,556 μ) cependant que celle de la rétine scotopique présente un maximum dans le vert-bleu (longueur d'onde 0,515 μ).

Le phénomène de Purkinje est caractéristique des rétines mixtes composées à la fois de bâtonnets et de cônes. Le pourpre rétinien des bâtonnets absorbe très peu de lumière d'une longueur d'onde supérieure à 0,620 μ (rouge); les cônes par contre sont beaucoup plus sensibles que les bâtonnets à la lumière rouge (et même aux éclairages de longueur d'onde plus brève). Cette différence de propriétés permet d'explorer isolement le fonctionnement des bâtonnets et celui des cônes dans les cas de rétine mixte. Il suffit pour cela de soumettre la rétine à des éclairages de longueur d'onde et à des états d'adaptation appropriés.

L'électro-rétinographie a confirmé la validité de la loi de Purkinje et permis de l'exprimer par une courbe. Si l'on reporte, en effet, les longueurs d'onde sur l'axe des abscisses et les valeurs de la réponse électrique rétinienne — l'amplitude du potentiel b, par exemple — sur l'axe des ordonnées, on obtient des courbes dont le maximum occupe une position différente dans le spectre suivant l'état d'adaptation de la rétine (Himstedt et Nagel 1901, Piper 1904, 1905, Brossa et Kohlrausch 1913).

Pour examiner la réception des couleurs, fonction essentiellement photopique, en rapport avec les cônes, il faut exclure dans la mesure du possible l'activité des bâtonnets qui, en produisant le phénomène de Purkinje, peuvent fausser l'interprétation de l'influence des couleurs sur l'ERG. Cette exclusion peut se faire à première vue par une simple adaptation à la lumière, qui a pour effet de détruire le pourpre rétinien des bâtonnets. Les potentiels positifs (b) produits essentiellement par ces récepteurs ne se manifesteraient plus, cependant que l'activité des cônes s'extérioriserait plus nettement sur l'ERG. On pourrait de cette façon préciser l'action des stimuli lumineux colorés sur l'ERG. L'expérience a montré toutefois que l'exploration des fonctions chromoréceptrices de la rétine chez l'homme n'est pas aussi simple qu'il le paraît à première vue. Chez l'homme, la faible proportion des cônes (par rapport aux bâtonnets) a pour effet que leur activité se manifeste à peine sur l'ERG même quand la rétine est adaptée à la lumière. Si leur réponse s'extériorise tout de même à la faveur d'une augmentation d'intensité du stimulus, elle peut être masquée alors par une réaction superposée des bâtonnets. Dans ces conditions il devient difficile de préciser chez l'homme, comme chez les mammifères à rétine du type E, l'action des stimuli lumineux colorés sur les récepteurs pendant l'adaptation à la lumière.

Groeppel, Haass et Kohlrausch (1938) ont étudié les corrélations entre les réponses de la rétine humaine à des stimuli monochromatiques et les sensations déterminées par ces mêmes stimuli (images consécutives). C'est toutefois à Adrian (1944, 1945) que l'on doit une analyse systématique des réponses électriques de la rétine humaine à des stimuli monochromatiques de brève durée. Il a individualisé deux composantes, l'une attribuée à un mécanisme photopique et l'autre à un mécanisme scotopique.

La *composante photopique* est caractérisée par une réponse diphasique brève composée d'une phase initiale négative suivie d'une phase positive. Elle est produite par des stimuli de lumière blanche ou par des stimuli monochromatiques de toutes couleurs à l'exception du bleu. On l'obtient avec plus de netteté quand on se sert de stimuli de lumière rouge et quand la rétine est complètement adaptée à la lumière. La réponse est également plus nette quand on excite la région centrale de la rétine; on pourrait conclure de ce fait qu'elle est produite surtout par l'excitation des cônes. Ce n'est pas absolument sûr, toutefois, puisque, nous l'avons vu, les bâtonnets peuvent réagir aussi à un stimulus lumineux intense. Cependant, quand le pourpre rétinien disparaît sous l'influence de l'adaptation à la lumière, la réponse de la rétine à une stimulation brève a une amplitude et une durée réduites qui l'apparentent à celle des cônes. Tout ce que l'on est en droit de dire, c'est que les réponses brèves obtenues après adaptation à la lumière, quelle que soit la proportion des cônes et des bâtonnets, est due à des photorécepteurs dépourvus de pourpre rétinien.

La *composante scotopique* est caractérisée par un potentiel lent et ample (300 à 400 μV) en réponse à des éclairages de toutes couleurs, à l'exception du rouge. Elle est particulièrement développée quand on se sert de stimuli de lumière bleue et que l'on éclaire les régions périphériques de la rétine. Elle ne se manifeste guère pendant l'adaptation à la lumière, mais apparaît nettement après adaptation à l'obscurité.

Enfin Adrian a obtenu une réponse complexe en appliquant des stimuli de lumière rouge orange, cette

riposte serait la resultante de la composante photopique rapide et de la composante scotopique lente

Les changements d'intensité du stimulus modifient l'amplitude mais pas la forme de la reponse quand il s'agit d'éclairages bleus et rouges Par contre quand les stimuli sont de longueurs d'onde intermediaires (vert jaune orange) la forme de la reponse peut varier suivant l'intensite et le degre d'adaptation à l'obscurité Adrian attribue cette variation au fait que la réponse est complexe et que ses deux composantes sont influencees differemment par ces diverses conditions L'augmentation de l'intensite fait apparaitre la composante photopique sous forme de potentiel positif de courte duree precede d'une deflexion initiale negative Ajoutons que la variation en fonction de l'intensité ou plutôt du produit intensité duree n'est decelable que pour les stimuli de breve duree Elle ne se manifeste plus quand le stimulus a une duree superieure a 1/15 sec pour la lumiere bleue et 1/20 sec pour la lumiere rouge La durée critique serait donc plus faible pour la lumière rouge que pour la lumiere bleue

A propos de l'influence de la couleur et de l'intensite du stimulus relevons encore que l'on a decrit a diverses reprises une elevation plus abrupte du potentiel b quand le stimulus a une longueur d'onde breve (Gotch 1904 Brossa et Kohlrausch 1913 1914 Smith 1939) Chez la grenouille cette influence de la longueur d'onde n'a pu être demontree toutefois que pour la retine adaptee a l'obscurite il est donc possible qu'elle soit une propriete du pourpre des bâtonnets (Granit et Munsterhjelm 1937 Granit et Wrede 1937) Il en va de même chez l'oiseau dont la retine est assez riche en bâtonnets pour produire le phenomene de Purkinje or tous les effets soi-disant specifiques des longueurs d'onde sur l'ERG de cet animal ont pu être reproduits par un choix approprie de l'intensite du stimulus (Graham et Riggs 1935 Granit 1942 b, Laurens 1932)

Experiences personnelles Il nous a paru interessant de contrôler l'influence de la longueur d'onde du stimulus sur la pente du potentiel b de l'ERG humain La pente etant exprimee par le temps de culmination il suffisait de comparer les temps de culmination des potentiels b produits par des stimuli lumineux de même energie mais de longueurs d'onde differentes (bleu vert rouge) Nous avons postule que les stimuli utilises avaient la même energie quand ils produisaient des potentiels b de même amplitude au cours d'une même experience de stimulation Nous avons donc groupe les potentiels b de même amplitude et examine si leur temps de culmination variait suivant la longueur d'onde du stimulus

Contrairement a ce que l'on aurait pu attendre notre analyse a montre dans 26 cas sur 43 une diminution nette du temps de culmination c'est-a-dire une pente plus raide du potentiel b sous l'influence des longueurs d'onde superieures (vert et rouge par opposition au bleu) Dans 13 cas sur 43 il n'y avait par contre aucune difference et dans 4 cas seulement une augmentation On peut conclure de ces observations que les stimuli de longueurs d'onde differentes n'exercent pas l'influence qu'on leur avait attribuee sur la pente du potentiel b quand on s'assure que les potentiels sont tous d'amplitude egale La pente ne devient pas plus abrupte quand la longueur d'onde diminue Nos experiences suggerent au contraire que si la longueur d'onde exerce une influence sur la pente du potentiel b le facteur brillance etant constant cette influence se traduit plutôt par une pente plus abrupte (3/5 des cas) quand la longueur d'onde du stimulus augmente C'est ce qu'illustre la fig 9 qui met en evidence la diminution du temps de culmination quand la couleur du stimulus passe du bleu au vert et surtout au rouge dans les 26 cas mentionnes plus haut

On peut se demander quel etait le *rôle de l'adaptation* dans ces experiences Rappelons qu'il s'agissait d'une stimulation lumineuse intermittente (1 eclair par seconde d'une duree de 1/10 sec) Or, ce mode de stimulation reduit progressivement nous l'avons dit l'amplitude des ERG de la serie en même temps qu'il allonge leur temps de culmination Ce fait confirme que la retine s'adapte a un eclairage d'intensite moyenne au cours de la stimulation intermittente Nous avons tenu compte de cette cause d'erreur et n'avons compare entre eux que des ERG ayant a peu pres le même numero d'ordre dans la serie

Il etait interessant enfin de comparer les temps de culmination des potentiels b produits par l'eclairement d'une region periphe-

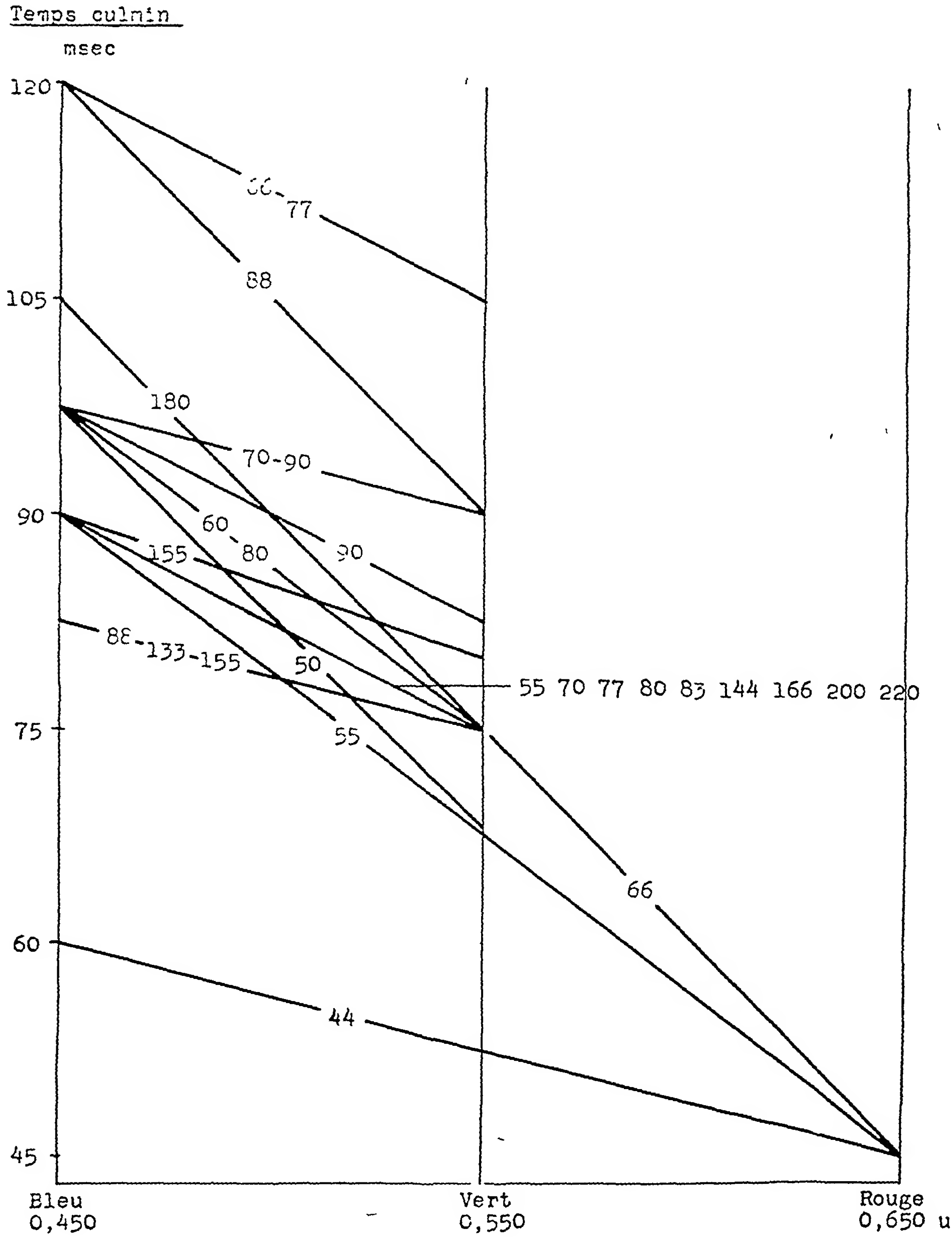


Fig 9

Variations du temps de culmination en fonction de la longueur d onde des stimuli lumineux Les points relies par une meme ligne se rapportent a des potentiels b de meme amplitude indiquee en μV par un chiffre Le temps de culmination diminue quand la longueur d onde augmente l amplitude restant constante

rique (60°) a ceux des ERG produits par la stimulation d une region plus centrale de la retine nasale (20°) ceci pour une longueur d'onde determinee et des potentiels de même amplitude

intermittente les stimuli de longueur d onde breve (vert-jaune et rouge) produisent des potentiels b plus rapides a pente plus abrupte que les stimuli de lumiere bleue A defaut du potentiel a non decelable sur nos ERG

Tableau IV — Variations du temps de culmination en fonction du lieu de la retine stimule et de la longueur d'onde des stimuli

Amplitude b µV	Bleu		Vert		Rouge	
	20°	60°	20°	60°	20°	60°
50	90	97	90	67	—	—
55	—	90	—	—	—	45
60	97	—	75	—	—	—
66	—	—	—	75	—	45
70	90	97	75	90	—	—
77	—	120	—	105	—	—
80	90	97	75	75	—	—
88	82	120	75	90	—	—
90	97	97	83	90	—	—

Du tableau IV il ressort que les temps de culmination des ERG produits par des stimuli de même couleur varient dans une certaine mesure suivant le lieu de la retine illumine Ils s'averent souvent un peu plus eleves quand on eclaire la region peripherique (60°) que lorsqu'on stimule une region plus centrale (20°) de la retine On peut conclure de ces observations que le territoire peripherique de la retine compose surtout de bâtonnets repond aux stimuli bleus et verts par des ERG un peu plus lents que ceux des regions centrales L augmentation relative du temps de culmination constituerait donc un critere de la composante scotopique en rapport avec l activite du territoire peripherique de la retine

Si l on considere enfin les valeurs absolues des temps de culmination on constate qu elles sont souvent plus faibles a 20 et 60° pour les stimuli verts que pour les bleus Le raccourcissement du temps de culmination est encore plus considerable quand il s agit de stimuli de couleur rouge 45 m sec pour le rouge au lieu de 75 m sec pour le vert et de 90 pour le bleu a 60° On peut conclure de ces rapports que pour l adaptation a un eclairage moyen realise par la stimulation nous sommes enclins a considerer cette diminution du temps de culmination comme un critere de la composante photopique activee par les stimuli de longueur d'onde superieure

Les ERG de la figure 10 mettent en evidence le même phenomene bien qu ils aient ete produits par des stimuli prolonges (2 sec) et non par des stimuli intermittents La pente est nettement plus raide sur les potentiels b provoques par les stimuli verts (0 550 µ) ou rouges (0 650 µ) que sur l ERG consecutif au stimulus de couleur bleue (0 450 µ) Les eclairages verts et rouges font donc ressortir la composante photopique de l ERG comme les eclairages de lumiere blanche Dans les conditions de nos experiences les manifestations de cette composante photopique se limitent au raccourcissement de la pente du potentiel b Le potentiel a ne se manifeste pas sur nos traces ce qui est peut-être dû au fait que nous n avons pas stimule de territoire plus central que sous un angle de 20° On hesite en effet a stimuler directement la fovea centralis a cause des reactions palpebrales de clignement particulierement vives quand il s agit de stimuli de lumiere rouge

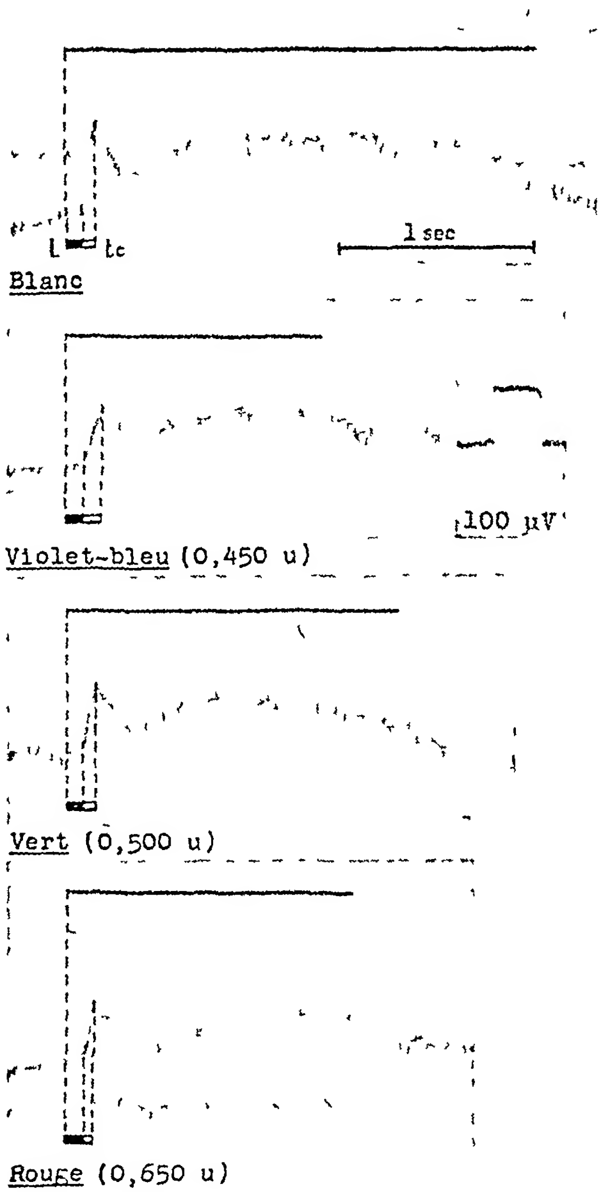


Fig 10

Influence de la longueur d onde sur le potentiel b de 3 ERG consecutifs a un stimulus prolonge (1-2 sec) Bien que l amplitude des 3 ERG inferieurs soit a peu pres egale leur pente s avere plus raide pour les stimuli de couleurs verte et rouge Id pour l ERG superieur produit par un stimulus de lumiere blanche Filtres Ilford

Exploration du fonctionnement des voies optiques par l'electro-retinographie et l'electro-encephalographie combinees

L'enregistrement simultane de l'EEG et de l'ERG chez l'homme permet de mesurer le *temps central* (Monnier et Boehm 1947a) Cette valeur que l'on obtient en deduisant le temps retinien du temps de blocage du rythme alpha est toutefois très variable Elle varie dans la même mesure que le temps de blocage, qui depend de facteurs individuels comme l'ont demontre Jasper et Cruikshank (1937) Il nous a paru opportun de choisir un critere plus constant pour contrôler objectivement le fonctionnement des voies optiques Le meilleur critere a cette fin paraît être le temps de latence des potentiels corticaux evoques par des stimuli lumineux (evoked potentials de Grey Walter, Dovey et Shipton 1946)

Avec Grey Walter nous avons eu l'occasion d'enregistrer recemment au Burden Neurological Institute de Bristol les potentiels corticaux evoques" par des stimuli lumineux de breve duree (10 micro-secondes stroboscope de Scophony) et, d autre part, la reponse de la retine aux mêmes stimuli En deduisant le temps retinien du temps de latence des potentiels corticaux "evoques' nous avons obtenu une valeur nettement plus stable que le temps central determine a partir du temps de blocage Cette valeur que nous proposons d'appeler, avec Grey Walter *temps retino-cortical* est de 50 m sec environ (± 15), cependant que le temps de latence des potentiels corticaux evoques atteint des moyennes de 95 a 125 m sec selon le sujet examine et les conditions de stimulation lumineuse

La mesure du temps retinien du temps retino-cortical et du temps de blocage du rythme alpha permettront a l'avenir de contrôler objectivement le fonctionnement du systeme optique chez l homme Nous aurons l'occasion d en apporter ici la preuve dans une publication ulterieure

CONCLUSIONS

Le perfectionnement des techniques de derivation d'amplification et d'enregistrement *oscillographique a rendu possible l'exploration* systematique de l activite electrique de la retine chez l'homme L *electro-retinographie* constitue aujourd hui comme l electro-encephalographie une methode d exploration en neuro-physiologie clinique dont il

nous a paru opportun de souligner ici l importance

La technique d *electro-retinographie perimetrique*, que nous avons mise au point avec F Boehm permet d examiner, chez l homme les variations de l electro-retinogramme (ERG) selon le lieu de la retine eclaire Elle permet aussi de varier la duree l intensite et la couleur du stimulus lumineux Les potentiels retiniens sont derives a l aide d electrodes impolarisables l une en contact avec la cornee l'autre fixee a la tempe Ils sont amplifies 2 000 000 de fois a l'aide d amplificateurs a couplage direct et enregistres avec un oscillographe cathodique

L analyse de plus de 1 800 traces a confirme que l *ERG normal de l homme* se caracterise par un potentiel a faible et inconstant un potentiel b dont les critères les plus sûrs sont le temps de latence la duree de la phase ascendante ou temps de culmination et l amplitude Le potentiel c est faible et inconstant quant au potentiel d extinction d il n est jamais positif Ces divers criteres permettent d assimiler l ERG de l'homme au type E de Granit comme celui de tous les mammiferes

L electro-retinographie binoculaire revele que l eclairement d un seul œil produit en plus de l ERG a l'œil stimule, une reaction consensuelle a l œil non eclaire Cette reponse consensuelle est semblable au potentiel c de l ERG nos examens de contrôle ont montre qu elle coincide avec le reflexe pupillaire consensuel

Le pouvoir de discrimination de la retine a l egard des changements brusques d eclairement peut être exprime objectivement par la *frequence de fusion* des potentiels b declenches par une stimulation intermittente Normalement cette frequence est superieure a 19 ou 20 eclairs par seconde et dans certains cas même superieure a 26 Pour cette valeur on constate une concordance entre le seuil de fusion determine objectivement et celui qui correspond a la disparition de la sensation de scintillement (flicker) La stimulation intermittente a pour effet de reduire progressivement des le debut l amplitude des potentiels b des ERG de la serie, cette diminution provient de l adaptation de la retine a un eclairage moyen sous l influence des premiers stimuli

L augmentation d *intensite* du stimulus lumineux a pour effet de raccourcir, d une part, les temps de latence et de culmination du potentiel b et d augmenter d autre part, l amplitude de ce potentiel

L'electro-retinographie perimetrique permet d'explorer la reactivite des divers territoires de la retine Elle montre que la stimulation des regions centrales (20°) produit des temps de latence et de culmination plus courts une amplitude du potentiel b plus elevee que les valeurs correspondantes des ERG declenches par la stimulation des regions peripheriques (60° champ nasal de la retine) Il est indispensable de connaître ces *variations en fonction du lieu de la retine stimule* quand on utilise l'electro-retinographie perimetrique a des fins diagnostiques, elles peuvent avoir des causes extra-retiniennes (diaphragme irien rapports entre la position des electrodes et la distribution des potentiels)

La stimulation de la retine avec des *eclairages de couleur differente* met en evidence deux composantes 1) une *composante photopique* caracterisee par une reponse breve particulierement nette quand on excite avec des stimuli de lumiere rouge la region centrale de la retine adaptee a la lumiere 2) une *composante scotopique* caracterisee par un potentiel b lent et ample tres prononce quand on excite avec des stimuli de lumiere bleue la region peripherique de la retine adaptee a l obscurite Les changements d intensite du stimulus peuvent modifier la forme de l ERG en faisant predominer l une ou l autre des 2 composantes lorsqu il s agit d eclairages de longueur d onde intermediaire (vert jaune orange) Nos observations ont montre que la forme de l ERG ne se modifie guere sous l influence des diverses longueurs d onde quand on a soin de ne comparer entre eux que des potentiels b de même amplitude La pente du potentiel b ne devient pas plus abrupte comme on l a

pretendu sous l'influence d une diminution de la longueur d'onde Dans 3/5 des cas, elle devient au contraire plus abrupte quand la longueur d onde du stimulus augmente (vert, rouge) Nous considerons cette diminution du temps de culmination sous l'influence des longueurs d'onde superieures comme une manifestation discrete de la composante photopique L'allongement du temps de culmination sous l'influence des stimuli de couleur bleue est au contraire un critere d'activite de l'appareil scotopique L'existence de cette composante scotopique, en rapport avec l'activite des bâtonnets, est prouvee en outre par le fait que le temps de culmination atteint son maximum quand on stimule la peripherie de la retine (60°) avec un faisceau de lumiere bleue

Signalons enfin que l'enregistrement simultane de l'ERG et de l'EEG permet de mesurer le *temps retino-cortical* Cette valeur que l'on obtient en deduisant du temps de latence des potentiels corticaux evoques par un stimulus lumineux (EEG), la latence du potentiel b determinée par l'ERG nous renseigne sur le fonctionnement des voies et des centres optiques

Par l expose de tous ces faits, nous esperons avoir demontre que l'electro-retinographie est une methode d'avenir en neurophysiologie clinique et que son developpement actuel infirme le pronostic pessimiste qu avaient emis a son sujet Kahn et Loewenstein pionniers de l'electro-retinographie chez l'homme en 1924 Wir sind der Meinung dass es wohl nicht wie wir anfangs hofften gelingen durfte die Aufnahme des menschlichen ERG zu einer Methode der Untersuchung des Auges auszubauen'

SUMMARY

A method of perimetric electroretinography is described, by means of which the action of duration, intensity, colour and location of the light stimuli on the human ERG can be studied

The analysis of more than 1,800 records confirms that the human ERG belongs to Granit s E type Its most characteristic feature is the b potential, quantitatively defined by the latency the duration of the ascendant phase or culmination time and the amplitude a and c potentials are small and often variable There is no positive off-effect

Binocular electroretinography elicits together with a normal ERG in the illuminated eye a consensual response in the other eye a reaction which seems to be coincident with the pupillary consensual reflex

The ability of the retina to differentiate light changes can be measured objectively by the fusion frequency of the small b potentials, elicited by flicker stimulation The fusion occurs normally at a rate of more than 19-20 often of more than 26 flashes per sec

The ERG in man varies not only with the duration but also with the intensity of the stimulus Increase of intensity produces a decrease in the latency and culmination time of potential b, as well as an increase in its amplitude

Perimetric electroretinography permits the study of the reactivity of various retinal areas and the objective delimitation of the visual field In the normal subject, stimulation of peripheral areas (60° nasal retina) produces an ERG with longer latency and culmination time, and smaller amplitude of the b potential than those elicited by stimulation of more central areas

Stimulation of the retina with monochromatic light stimuli elicits 1 A photopic component, particularly marked when the central area of the retina, adapted to light is stimulated with red light 2 A scotopic component with slow and broad b' potential, particularly marked when the peripheral area of the retina adapted to darkness, is stimulated with blue light This scotopic response shows a longer culmination time when the wave-length of the stimulus decreases, it reaches its maximum when the peripheral retina is stimulated with blue light

Simultaneous recording of ERG and EEG permits measurement of the retino-cortical time, as well as of the alpha-blocking time

The retino-cortical time that is the latency of the evoked potentials is more constant than the alpha-blocking time being only 50 m sec (± 15) Measurement of the retinal time, the retino-cortical time and the alpha-blocking time can provide useful information about the functional state of the various sections of the visual tracts and centres

---

Qu il nous soit permis d exprimer ici notre gratitude au Dr Grey Walter pour ses précieux conseils a M F Boehm et Mlle M -L Fleissig pour leur patiente collaboration

BIBLIOGRAPHIE

A — Les publications relatives a l *électro rétinographie chez l animal* citées dans notre travail sont trop nombreuses pour figurer toutes dans ce rappel bibliographique On en trouvera les références dans les monographies suivantes

GRANIT R *Sensory Mechanismus of the Retina* with an appendix on electro retinography London New York Toronto 1947 Oxford University Press 412 pp

KOHLRAUSCH A Elektrische Erscheinungen am Auge In *Hdb d norm u pathol Physiol* Bethe Bergmann, 1931 *12/2* 1393-1496

KOHLRAUSCH A Die elektrischen Vorgange im Sehorgan *Kurzes Hdb d Ophtalm Schieck u Brückner* 1932 2 118 171

SCHAEFFER H *Elektrophysiologie II Die Elektrophysiologie des Gesichtssinnes* Wien F Deuticke 1942 193 232

B — Publications relatives a l *électro rétinographie chez l homme* et aux questions connexes

ADRIAN E D Rod and cone responses in the human eye *Nature* 1944 *154* 361-362

ADRIAN E D The electric response of the human eye *J Physiol* 1945 *104* 84 104

BERNHARD C G Contributions to the neurophysiology of the optic pathways *Acta Physiol Scand* 1940 *1* Suppl I

BOEHM F SIGG B et MONNIER M Elektroretinographische Untersuchungen am wachen Meerschweinchen *Helv Physiol Acta* 1944 2 481 493

COOPER S CREED R S et GRANIT R A note on the retinal action potential of the human eye *J Physiol* 1933 *79* 185-190

CRUIKSHANK R M Human occipital brain potentials as affected by intentity-duration variables of visual stimulation *J Exp Psychol* 1937 *21* 625 641

DEWAR J The physiological action of light *Nature* 1877 *15* 433-435 453 454

GRANIT R Isolation of components in the retinal action potential of the decerebrate dark-adapted cat *J Physiol* 1932 *76* I P

GRANIT R *Sensory Mechanismus of the retina* with an appendix on electro retinography London New York Toronto 1947 Oxford University Press 412 pp

GROPPEL F HAASS F et KOHLRAUSCH A Aktionsströme und Gesichtsempfindungen des menschlichen Auges *Z Sinnes physiol* 1938 *67* 207-226

HARTLINE H K The electrical response to illumination of the eye in intact animals including the human subject and in decerebrate preparations *Amer J Physiol* 1925 *73* 600 612

JASPER H H Cortical excitatory state and synchronismus in the control of bioelectrical autonomous rhythms *Cold Spring Harbor Symp Quant Biol* 1936 *4* 300 338

JASPER H H et CRUIKSHANK R M Electro encephalography II Visual stimulation and the after-image as affecting the occipital alpha rhythm *J Gen Psychol* 1937 *17* 29 48

KAHN R H et LOEWENSTEIN A Das Elektroretinogramm *Graefe s Arch Ophthalm* 1924 *114* 304-331

KARPE G The basis of clinical electroretinography *Acta Ophthal Kbh* 1945 *Suppl 24* 1-118

KOHLRAUSCH A Elektrische Erscheinungen am Auge *Hdb norm path Physiol* Bethe Bergmann 1931 *12/2* 1394-1396

KOHLRAUSCH A Die elektrische Vorgange im Sehorgan *Kurzes Hdb Ophthal* Schieck u Bruckner 1932 *2* 118-171

MONNIER M a) L electro retinogramme (ERG) chez l homme *C R Soc Biol Paris* 1946 *140* 231-233

MONNIER M b) Les manifestations electriques consensuelles de l activite retinienne chez l homme (Electroretinographie binoculaire) *Experientia* 1946 *2* 190 191

MONNIER M L électro retinogramme (ERG) de l homme *17th Internat Physiol Congress Abst of Comm* 1947 201-202

MONNIER M et AMSLER M Examen objectif de la fonction retinienne par l electro retinogramme dans un cas de retrecissement concentrique du champ visuel *Ophthalmologica Acta (Basel)* 1945 *110* 225-245

MONNIER M et BOEHM F Technik der Elektroretinographie beim Menschen *Helv Physiol Acta* 1945 *3* C25 C27

MONNIER M et BOEHM F Objektivierung der Lichtrezeption in der Netzhaut durch das Elektroretinogramm beim Menschen *Helv Physiol Acta* 1945 *3* C39 C51

MONNIER M et BOEHM F Lichtempfindungen und bioelektrische Erscheinungen der Netzhaut auf Lichtreize beim Menschen (Elektroretinogramm) *Schw Med Wschr* 1946 *76* 161

MONNIER M et BOEHM F a) Prufung der Leistungs fahigkeit des optischen Systems durch kombinierte Elektroretinographie und Elektroencephalographie beim Menschen *Helv Physiol Acta* 1947 *5* C34-C35

MONNIER M et BOEHM F b) Beiträge zum Elektroretinogramm des Menschen I Perimetrische Elektroretinographie *Helv Physiol Acta* 1947 *5* 205-224

MONNIER M et JEANNERET R L Contrôle objectif de la conductibilite des voies optiques centrales par l electro-retinographie et l electro-encephalographie combinees *Ophthalmologica Acta (Basel)* 1947, *113* 1-11

RIGGS L A Continuous and reproducible records of the electrical activity of the human retina *Proc Soc Exp Biol & Med* 1941 *48* 204-205

SACHS E Die Aktionsstrome des menschlichen Auges ihre Beziehung zu Reiz und Empfindung *Klin Wschr* 1929 *8* 136 137

WALTER W GREY The Technique and Application of Electroencephalography *J Neurol Psychiat*, 1938 *1* 359-385

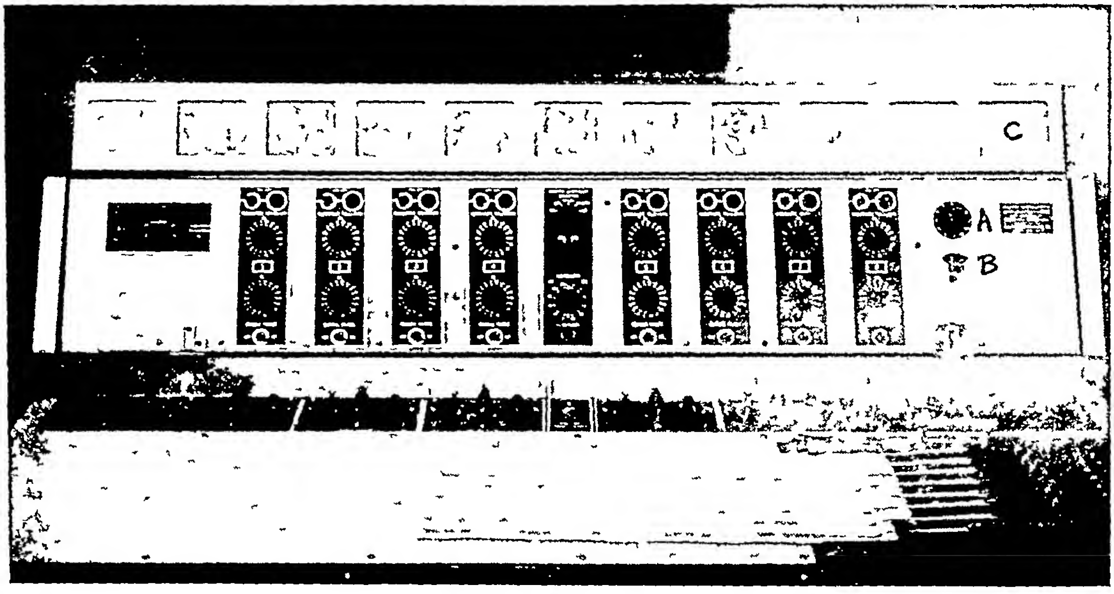
WALTER W GREY DOVEY, V J et SHIPTON H Analysis of the electrical response of the human cortex to photic stimulation *Nature* 1946 *158* 540-541

TECHNICAL NOTES

AN AUTOMATIC ELECTRODE COMBINATION SELECTOR SWITCH

R G Bickford, M D
Section on Physiology Mayo Clinic
and Mayo Foundation
Rochester, Minnesota

In spite of the fact that automatic electrode selector switches have been incorporated in standard electroencephalographic equipment (Grass Offner) in the past technicians have been reluctant to take advantage of this system This has doubtless been due to the fact that the particular combinations chosen by the manufacturer have frequently failed to match the requirements of the individual laboratory A switch wired so that alterations could be easily accomplished and incorporating a visual indicator has been used in this laboratory for several months There has been a considerable saving in recording time as the switching operations required to change a combination are reduced from sixteen to one Fatigue of the operator from constant turning of the switches is much reduced and tendency to error almost eliminated For the latter reason the training of new technicians is facilitated



Construction (see photograph)

The assembly which has been incorporated into a Grass 8 channel electroencephalograph consists of three parts An on off connector switch (B) an electrode selector switch (A) and a row of visual indicator panels (C)

The connector switch is a 17 pole double throw switch of the wafer type whose function is to connect the 16 input grids either to the selector switch or to the individual panel switches normally employed The 17th pole switches in the panel lighting behind the head diagrams of the visual indicator (C)

The electrode selector switch (A) is a 17 pole 11-position switch mounted parallel to the back of the preamplifier panel through a right angle gear drive By connecting the individual electrode leads to appropriate positions on the selector switch any desired electrode combination patterns can be obtained The

17th wafer serves to switch the lights at the back of each head diagram so that for any particular switch position the corresponding head diagram is illuminated

The visual indicator panel (C) carries 11 sections with windows corresponding to each position on the selector switch Each window takes a standard lantern slide showing a head diagram with the laboratory code on the right hand side and backed by a layer of semi-transparent white paper Behind each window there is a six volt light bulb supplied from the storage battery and switched by the 17th wafer of the selector switch The 17th wafer of the connector on-off switch breaks the panel lighting circuit when in the off position thus indicating clearly which switching system is in use

It has been found necessary to employ only nine of the possible eleven electrode combination patterns in the routine work of this laboratory

A NEW NASOPHARYNGEAL LEAD[1]

PAUL D MACLEAN, M D [2]

A nasopharyngeal lead for recording potentials at the base of the brain has been designed which combines the following advantages (1) ensures good recording without baseline sway (2) requires no co-

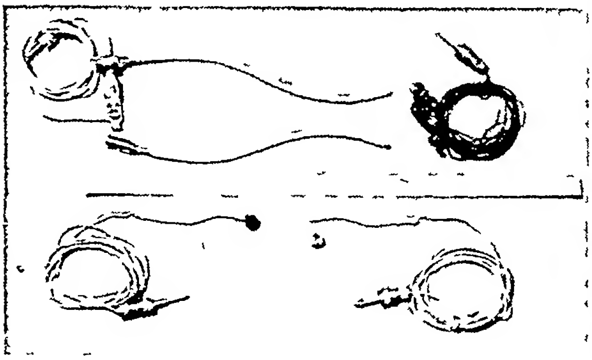


Fig 1

cainization of the nasal passages (3) may be installed in a matter of seconds without the use of nasal speculum or head mirror (4) is comfortable for the patient (5) two such leads may be used one on each side of the nose for bipolar recordings from the base of the brain (6) allows the subject of a sleep experiment to sleep with two such leads in place for a period of several hours

The electrode is made of silver tubing 12 5 cm long and 2 5 mm in diameter which is soldered to a needle shank (see upper half of Fig 1) A silver tip with a spherical surface for contact with the mucous membrane is pegged into the opposite end of the tube The electrode is insulated save for the tip and needle shank by two or more thin coatings of a corrosive-resistant white paint such as Tygon Before

Fig 2

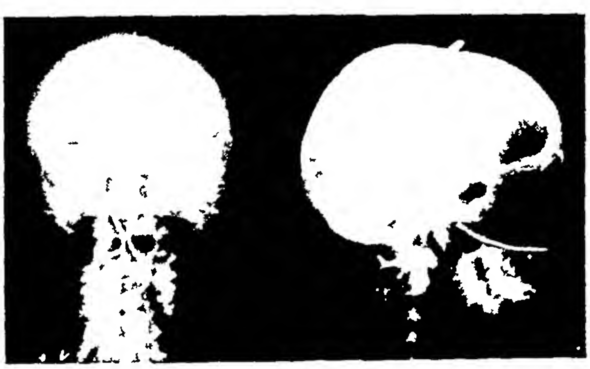
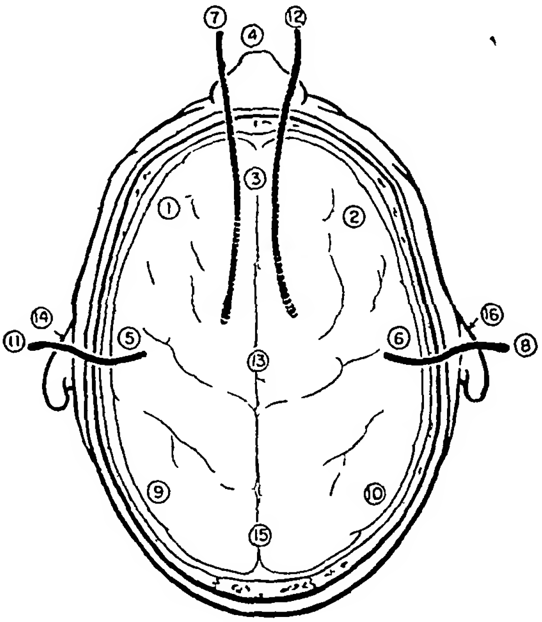


Fig 3

1 Originally presented as an exhibit at the Second Annual Meeting of the American Electroencephalographic Society Atlantic City June 12 1948

2 Research Fellow in Psychiatry Massachusetts General Hospital and Harvard Medical School

the tube is dipped in the paint it should be gently roughened by emery paper to provide a good adhering surface The distal half of the tube is given a round bend (with a radius of about 8 cm) to allow the tip to reach the posterolateral nasopharynx The proximal half is bent to an equal degree in the oppo



places the tip of the patient's nose upwards and directs the electrode so that its convexity will pass along the floor of the nose In this way the turbinates are avoided Thereafter the electrode usually guides itself until it comes to rest firmly in the vault of the nasopharynx At this time the tip may be rotated lateralwards or medialwards as desired Connection of the electrode and the lead wire to the box is afforded by a #45 clip which bites into the needle shank *The weight of this clip adds to the inertia of the electrode and helps to stabilize it and keep it in place* further stability is given by anchoring the lead wire to the cheek by a piece of adhesive tape It is more comfortable for the patient if the clip is fastened to the needle shank before the electrode is installed A small amount of vaseline applied to the tube of the electrode facilitates its passage

Figure 2 shows a subject with two nasopharyngeal leads in place [1] Each lead is rotated laterally about 45° and in this position points towards the petrous portion of the temporal bone X-ray (Fig 3) and anatomical studies indicate that the tip of the lead is not more than 2 cm from the anterior mesial surface of the temporal lobe possibly closer The tips of the two leads when well placed are about 3 cm apart

The resistance between two nasopharyngeal leads or between a nasopharyngeal and any other electrode on the scalp usually measures less than 6500 ohms

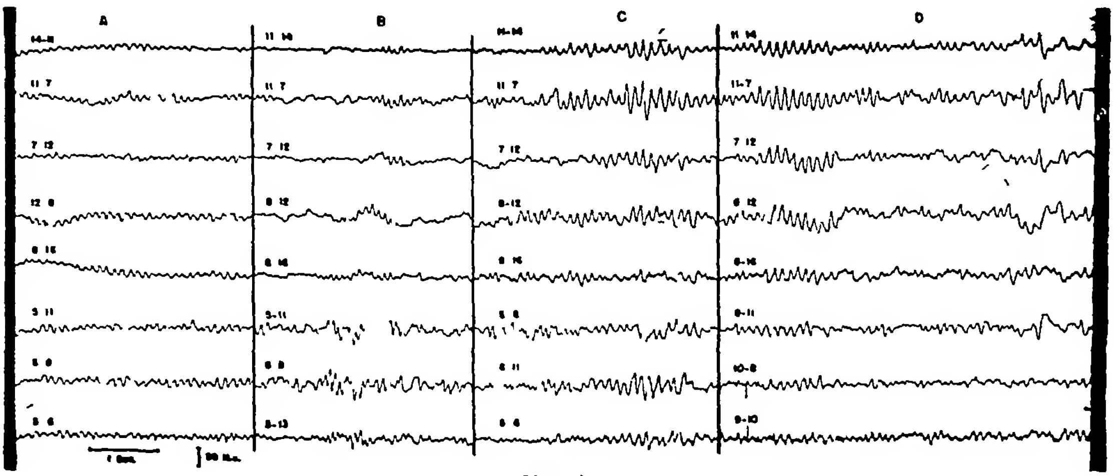


Fig 4

site direction This latter curvature not only serves to avoid pressure in the region of the patient's external nares but also allows the operator to judge the proper plane for placing the tip

Inserting the electrode The patient is placed in the supine position for examination The operator dis

All recordings (to date 110) made by the technique described here have been uniformly successful The tracings involving the nasopharyngeal leads generally cannot be distinguished in quality from

1 The second electrode may be made longer by 1 5 cm so that the clips do not interfere with each other

those taken with the routine scalp leads (Figs 4 5) A ten-year old boy has submitted quietly to the placement of two electrodes in his nose elderly patients do not object to the procedure No patient has refused re-examination with this technique Some patients have had as many as five recordings Patients are able to sleep with the two leads in place figure 5 illustrates a sleep record

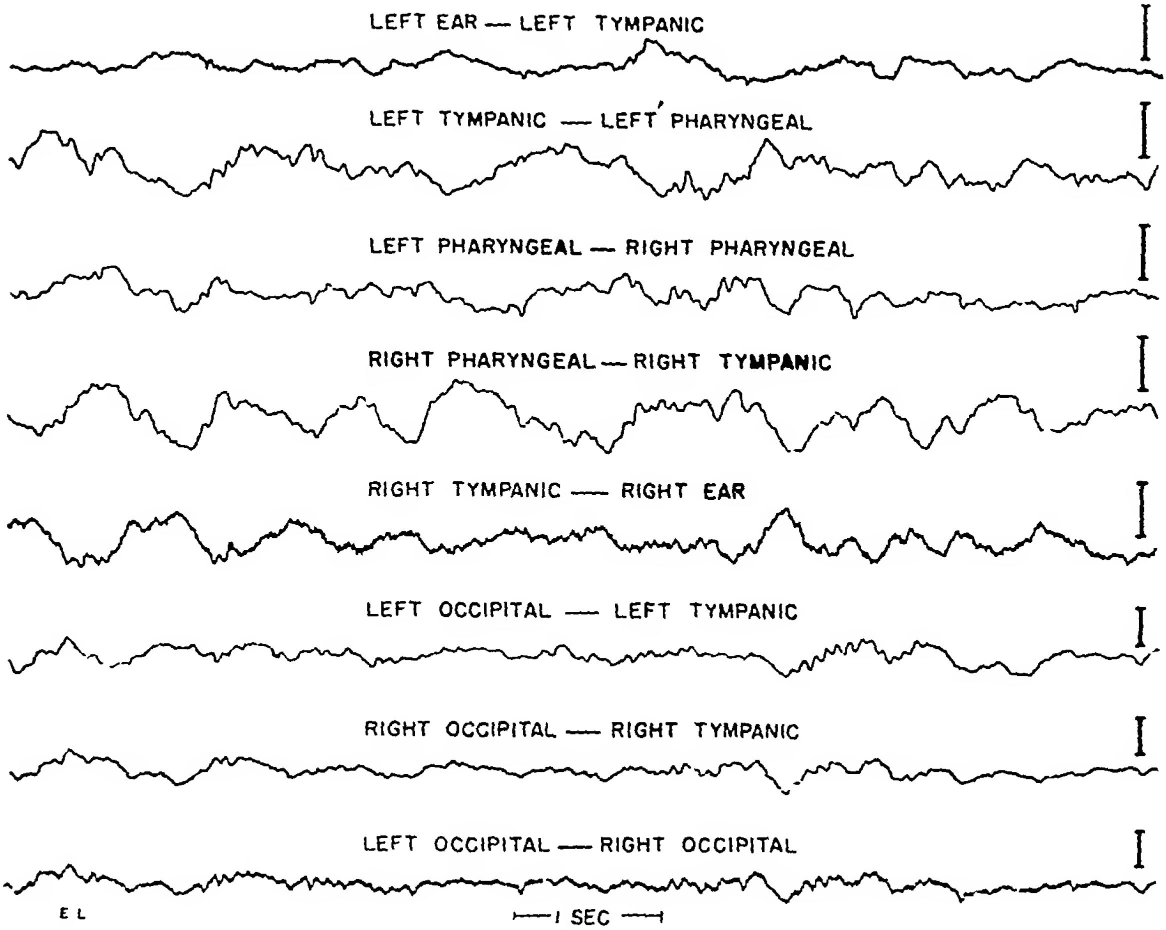


Fig 5

A TYMPANIC LEAD

ALEJANDRO P ARELLANO Z[1]

The technique consists in placing a special type of electrode in each tympanic region so that it makes contact with the tympanic membrane in such a way that the local resistance is adequately low The electrode is a silver tube of 6 cm in length and 2 5 mm in diameter which is bent somewhat in the form of an S so as to conform to the contour of the external auditory canal (see lower half of figure 1 Figures same as previous note) A lead wire is soldered to one end The rest of the electrode is insulated except at the tip by corrosive-resistant paint such as Tygon A ball of soft felt 7 mm in diameter is attached to the non-insulated end where two small holes provide the passage of stitches for its attachment

The patient lies in the supine position and the ears are inspected with an otoscope and if necessary any large accumulations of cerumen are removed The external auditory canal is strained by appropriate

[1] Research Fellow of National Institute of Mental Health U S Public Health Service From the Medical School of University of Lima Peru

manipulation of pinna and the electrode whose felt tip has been soaked in normal saline is inserted until the patient feels a slight momentary pain At this time the electrode should have passed a distance of about 3 5 cm from the tragus and lie next to the tympanic membrane

Ordinarily the resistance between two tympanic leads or between a tympanic lead and a reference lead is less than 20 000 ohms Should the resistance be unduly high artifacts will appear This situation usually can be remedied by injecting a few drops of normal saline through the hollow tube of the electrode The topographic placements of the basal tympanic leads and their relations with other leads are shown in the X-ray picture of the skull taken with them in place (Fig 3) They seem to be the closest leads to the middle and posterior cranial fossae which are available with an intact skull

The recordings obtained (Fig 4) of different linkages between the basal leads themselves (between tympanics tympanic to nasopharyngeal leads etc) and combined with the scalp leads are of as good quality as those from the usual scalp recordings

Up to the present time over 40 recordings have been made with this technique Patients tolerate the procedure well even for as long as two hours and during sleep There has been no objection to repeating the procedure This technique has not been used on patients with perforation of the tympanic membrane otitis or any other similar condition

DISCUSSION

The 2 tympanic leads and the 2 pharyngeal leads and the right and left ear lobes form a transverse line of electrodes that cover the base of the brain fairly satisfactorily Examples of tracings obtained from these leads are shown in figures 4 and 5 Such basal recording particularly when supplemented with the usual scalp leads is useful in localizing electrical activity from the deeper structures and has been of some help in localizing tumors in these area The EEG in migraine and hypertension is being investigated by means of these techniques

The authors wish to thank Dr Stanley Cobb and Dr Robert S Schwab for the help and guidance in this work and Mr James Casby for his technical assistance

From the Brain Wave Laboratory Massachusetts General Hospital Boston 14 Mass

---

A METHOD OF ANALYSIS OF SEIZURE PATTERN AND ELECTROENCEPHALOGRAM [1]

A CINEMATOGRAPHIC TECHNIQUE

JOHN HUNTER and HERBERT H JASPER

The accurate observation of the sequence of events that occur in an epileptic seizure is as important to the clinician as is the accurate localization of the onset of the abnormal electrical activity of the brain to the electroencephalographer

To the neurosurgeon a precise correlation of both these factors can be a deciding issue in the assessment of the value of cortical surgery in intractable epileptic problems

Since the technique of activation of the EEG by various methods (Cure (1) Walker (2)) has come to be both practicable and reliable the clinical and EEG manifestations of a seizure onset — or even of a seizure itself may now be reproduced under controlled circumstances with relatively little inconvenience to patient or laboratory

As a further aid to this problem as it presents in epilepsy there has been developed a method of recording these observations in their correct temporal sequence and in correct relationship to each other utilizing 16 mm cinematography in a special optical system

At the 96th Annual Meeting of the American Psychiatric Association in 1938 Schwab (3) presented a photographic method of recording patient and EEG record on one film This was obtained by using two separate 16 mm films in two cameras and after processing having a composite duplicate made Synchronization was effected by special synchronizing marks on each film

Subsequent to this Stevenson (4) utilized a split frame procedure on a single film By means of masks it was possible at a later date to place the image of the EEG record above or beside the image of the patient accurate synchronization by this procedure was difficult

The method now presented consists of photographing the patient and the EEG record at the same time on the same frame of a 16 mm film thus any errors in synchronization are entirely eliminated

---

[1] From the Department of Neurology and Neurosurgery McGill University and the Montreal Neurological Institute Reprint no 288

TECHNIQUE

The optical system employed is shown in figure 1 The patient and the recording apparatus are in separate rooms between which is an observation window The image of the patient is obtained from the large mirror (5' x 3') above the bed By means of a 12 inch diameter plano-convex clear glass condenser lens and a surface silvered mirror (18" x 12') above it the image of the pens and some 5 inches of record (using 4 pens) is obtained from the small rectangular mirror (2" x 1½') fastened to the plate glass observation window By altering the height of the lens in respect to the paper the number of pens photographed may be varied from two to six or more

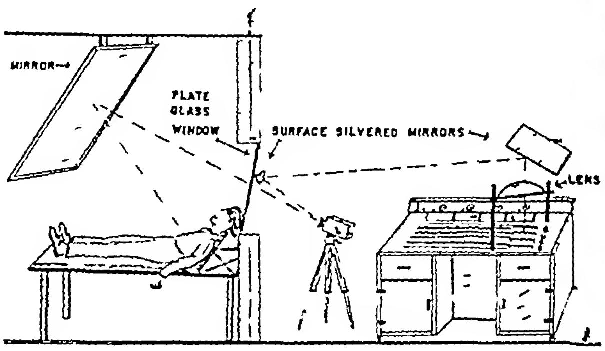


Fig 1 — Schematic drawing of optical system

After composition of the patient in the camera viewer so as to include the full body — or if required only head and neck — the small mirror on the window is so adjusted that its image of the pens is caused to occupy a section of the frame which is not being utilized by the image of the patient It must be noted that a system such as this is not corrected from left to right

The focal distance used in the above procedure was approximately 15 feet at which point both images were brought into focus The lighting of correct colour temperature was balanced so that equal illumination fell on both patient and record Colour film only was used and exposures were made at 24 frames per second with a 1 inch coated lens using an aperture of f 4

A small coloured signal light placed to the side of the pens (Fig 2 s) was wired in such a way that when the contact switch held by the patient was open the light came on by this means it was possible to record a loss of voluntary effort or period of unresponsiveness For purposes of noting hyperventilation commencement of injection speed and strength of injection etc a series of glass plates (7 x 5) with opaque printed writing were swung in from left to right between the record and the condenser lens without obscuring the record

Fig 2 — 16 mm frame during petit mal seizure, coloured signal light s is on indicating release of hand contact switch

The use of such a system as this makes possible the evaluation of many factors important in epilepsy and which otherwise would be frequently missed because of difficulties in observation and recording By choice of a different set of lens the proportion of the frame occupied by patient and EEG record can be modified

REFERENCES

1 Cure C Rasmussen T and Jasper H Metrazol activation of seizures and electroencephalo graphic disturbances in epileptic and control sub jects *Arch Neurol & Psychiat* 1948 *59* 691-717

2 Kaufman C Marshall W and Walker A E Activated Electroencephalography *Arch Neurol & Psychiat* 1947 *58* 533-549

3 Schwab R Personal Communication

4 Stevenson C Personal Communication

SOCIETY PROCEEDINGS

Edited by John Knott

THE EEG SOCIETY [1]

(The Electroencephalographic Society)
Great Britain

Spring Meeting May 1948
The Burden Neurological Institute

Presidential address — Prof F L Golla

"The Role of the Electroencephalographer in Applied Neurophysiology"

COMMUNICATIONS

1 Relationship between EEG and Autonomic Changes during Induced Hypoglycaemia — D Hill, P St John Loe, J Theobald and M Waddell.

In 1943 Heppenstall and Hill reported to this Society the comparison between the EEG changes to induced hypoglycaemia in normals and in chronic schizophrenics The results indicated a hyporeactivity of the EEG in the latter but could not be extended because of the factor of insulin resistance (failure of the blood sugar to fall after intravenous insulin) met in many schizophrenics The present communication is concerned with an extension of these studies to include the changes in heart rate and galvanic skin resistance related to the fall of blood sugar after a standardised dose of intravenous insulin and the time of change of cortical rhythms during this process Controls have been examined and 4 types of response have emerged The methods and technique will be presented Each type of response represents a pattern involving relationships between

(a) a falling blood sugar curve and a tendency to homeostatic rise in blood sugar at ± 25 minutes after injection

(b) the first appearance of slow-wave activity in the EEG

(c) rise in heart-rate and fall in galvanic skin resistance as indicators of activity of the sympathetic adrenalin system

The four types of response have been designated types A B C and D Comparison of the patterns found in controls and psychotic patients show that the method is valid for demonstrating differences in the central homeostatic mechanisms in psychotic subjects and can be used to evaluate the earlier results

[1] Secretary Dr W Grey Walter Burden Neurological Institute Bristol England

2 Underrichts's Myoclonic Epilepsy in Identical Twins — D S Fairweather, H J L O'Sullivan and W Grey Walter

The patients are twin sisters aged 23 years and were admitted to Stoke Park Colony in September 1938 They began with mild myoclonic attacks when aged 13 and shortly afterwards developed grand mal attacks The familial nature of the condition is indicated by the fact that their mother was married twice and has 2 families 4 in the first and 9 in the second None of the first family were affected by this condition but 5 out of 9 of the second family were affected The father's aunt and 2 cousins were also similarly affected The elder 2 children aged 29 and 27 of the family of 9 are males and unaffected the third child is Mary aged 26 who has been in bed for 18 years and was at Warlingham Surrey for 14 of those years She is at present at Hatton Warwick with myoclonic epilepsy The fourth child Alfred is aged 24 and has been at Hatton for 7 years also with myoclonic epilepsy The present cases Lily and Violet aged 23 are the 5th and 6th in the family Then follow 2 unaffected daughters aged 22 and 20 and lastly Jean aged 19 who was at Lingfield Epileptic Colony for a time with myoclonic epilepsy In Jean's case the parents attribute the epilepsy to an accident when she was aged 5 in which she fractured her skull and was unconscious for 4 days She is now bedridden at home The inheritance of the condition is usually considered to be Mendelian recessive The myoclonic attacks are variable in their range severity and frequency They include generalised muscular spasms localised muscular contractions affecting one or two limbs and various kinds of tics The average frequency of their major epileptic attacks is one per month Their mental ages are for Lily 6 6 I Q 46 and for Violet 6 8 I Q 48 Excitement and emotional stress appear to aggravate the severity of the myoclonic attacks Their mental state is generally one of mild euphoria with occasional lapses into tearfulness and general irritability

Examination of the CNS discloses the following abnormalities in addition to the myoclonic attacks in the case of Lily a convergent strabismus some degree of generalised muscular hypotonia slight ataxia and *when the attacks are severe astasia-abasia* In the case of Violet signs are less marked and more fluctuant but show similar features

Evidence for the twins identity is furnished by their fulfilling Stocks criteria and by the identity of their blood groups

Electro encephalograms have been taken from both twins on several occasions The records will be displayed They are similar but not identical in the two cases The usual features found in myoclonic epilepsy are well represented Of particular interest is the response to photic stimulation violent rhythmic jerkings are evoked immediately by even quite faint flashes of light and generalised convulsions supervene if the stimulation is continued for more than a few seconds The jerkings are accompanied by extremely large electrical discharges

The genetic origin of the disturbance in these cases, and the location of the lesions support the hypothesis put forward previously of the nature of photogenic epilepsy

3 Experimental Homeostat — W R Ashby

If any arrangement of neurones includes a circuit so that impulses from any cell can ultimately return to that cell then the circuit tends to become self-activating and may develop oscillatory properties Conversely the occurrence in a dynamic system of steady oscillations is strong evidence that some circuit is involved Recent work has suggested that neuronic systems arranged in circuit form may be of importance in several ways in normal functioning (Lorente de No) in the alpha and other rhythms in interaction with the environment (Ashby), and in pathological conditions such as epilepsy

Systems containing circuits will usually be either stable oscillating or unstable When stable they show interesting self-preservative and homeostatic activities When oscillating they will be of interest to the electroencephalogist When unstable they show features possibly related to epilepsy and other deviations from normality

The mathematical treatment of such systems *is* straight forward in the simple (linear) cases but becomes impossibly laborious when more complex The Homeostat is a machine designed so that it can be set to copy the essential features of any given circuit it will then show by its behaviour how such a system would behave It is a type of calculating machine as after it has been set appropriately for some specific question the answer is supplied by its behaviour The answer will usually be in qualitative form e g that the system is stable or that it will oscillate with increasing amplitude Its aim is primarily to give qualitative information about a great variety *of possible systems rather than to give minutely de*tailed information about any particular one

Construction

It consists of units, each of which accepts varying D C currents from the other units, while it also emits a varying D C current which it sends to the other units

The behaviour of each unit is indicated by a magnetic needle The currents coming from the other units traverse coils around the magnet and so produce a combined effect on it making it turn There is a trough of water with electrodes at the ends so that there is a varying potential along the length of the trough The magnet carries a wire which dips into the trough so the wire picks up a potential which *varies as the magnet turns This potential is trans*ferred to the grid of a valve thus controlling the anode current which is the unit s output (This output current then goes to another unit where it circulates round the magnet and so on)

The operator can pre-set the magnitude and sign of the effect which each unit has on each other unit

Built in are uniselectors, arranged and wired so that they will provide over 5×10^{10} combinations of such settings for sampling purposes

Theory

It can be shown that such a system, under certain conditions behaves in accordance with the equations

$$\frac{dx_i}{dt} = a_{i1}x_1 + a_{i2}x_2 + \quad + a_{in}x_n \quad (i = 1, \quad n)$$

As the *a* s can be set directly on the machine it can be set to copy any other system whose behaviour is covered by similar equations To a first approximation this covers all dynamic systems whatever

Uses

(1) The stability oscillation etc of a given system can be found at once

(2) It shows the effects of various types of feedback whether simple multiple, or more particularly, *patterned in some complex way*

(3) The interactions between a stable and an unstable system can be observed under various conditions

(4) Large numbers of related circuits can be tested in order to find the proportion having some particular feature e g the proportion of unstable wholes which occur when two stable systems form random interconnexions

(5) It demonstrates various fundamental properties of dynamic systems e g

(a) that two systems each intrinsically stable may become unstable when joined

(b) that joining units can only decrease stability

(c) that if part of a stable system is slowed down the whole may become unstable

(d) that two systems may form a whole which is stable if they are joined one way but unstable if joined in another way

etc

(6) Various physiological and pathological features can be imitated and their effects on reverberating neuronic systems studied e g the effects of increasing threshold of strychnine of parts becoming slower in action or of parts becoming non-reactive (e g anaesthetised anoxaemic or dead) etc

DEMONSTRATIONS

1 A New Electromagnetic Oscillograph — A Remond and A Ubersfeld

This instrument was shown at the International Meeting in July but only a few people could see it working at that time It consists of four stationary coils and a soft iron moving armature The coils are disposed at the corners of a rectangle those at opposite corners are connected in series so that 2 pairs of magnetic poles are produced with like poles adjacent to each other Each pair of coils is connected directly to the anode of one side of the output stage of a class A push pull amplifier (EFF51) There is thus no need for permanent magnets or energising coils

As a result of the push pull operation the total magnetic field acting on the armature is unvarying but its position is altered when a signal is applied to the amplifier input

The coils have a resistance of 5000 ohms per pair and a deflection of 20 mm is obtained with a pen 7 cm long the standing current being 10 mA Sensitivity is constant up to a frequency of 100-150 c/sec and the dimensions of the instrument are such as to permit multi channel construction The control spring tension is adjustable to permit variation of characteristics

2 "Utility" Amplifiers and Recorders Designed at the BNI

The price of commercial apparatus remaining obstinately high and its performance mediocre the development of cheap adequate equipment has been undertaken

The design is based on a frame rather than a chassis Light alloys and non-ferrous materials are used The circuit is basically the same as that described for a *Portable Equipment in Electronic Engineering* Valves used are EF37 EF50 EL37, (Mullard) Units are available in either 2 channel (portable) or 6 channel (static) form Separate frames are used for pre amplifiers control unit power amplifiers power pack The performance is up to the International Specification Special features are accessibility robustness Master gain filter and time constant controls The recorders are moving iron balanced armature rubber suspended Without case work or paper drive the complete amplifier and recorder set is sold at £350 for a 6 channel unit by Mr A R Michell of Shrewsbury

A utility Analyser and Toposcope are in course of development

ORDINARY MEETING, September, 1948
National Hospital, Queens Square, London

COMMUNICATIONS

1 The Spontaneous Variability of the EEG in some Schizophrenics — Denis Hill and D Rowntree

The patterns of the EEG in the large clinical group known as schizophrenics show greater variations than in any other group of patients The types of EEG found will be reviewed The greatest incidence of abnormal patterns is found among catatonic schizos Two findings in this group will be considered (A) patterns suggesting epileptic activity and (B) moderate voltage bilaterally synchronous slow activity mainly at 4-6 c/sec Both these abnormalities show considerable spontaneous variability which tends to be related to changes in the clinical condition of the patients

2 Effect of DFP (Di isopropyl fluorophosphate) on the EEG of Psychotics — D Rowntree and S Nevin

DFP a potent anti-cholinesterase has been shown to inhibit irreversibly the cholinesterase with which it comes in contact

By means of this drug, therefore an increased concentration of acetyl-choline can be maintained in the tissues over long periods

Parasympatheticmimetic effects are produced but mental neurological and EEG changes indicate a significant effect on the central nervous system

The EEG changes consist of

(1) Lowering the amplitude of all rhythms with tendency for the alpha rhythms to disappear

(2) Lowering the frequency of the alpha rhythm (up to 2 c/sec)

(3) Appearance of slow rhythms — usually of low voltage generalised but tending to be most evident in parietal areas

(4) Disorganisation of the record

(5) Increased instability on hyperventilation with comparable blood sugars

With equivalent experimental conditions of dosage cholinesterase inhibition etc these changes are much less marked in the schizophrenic group Schizos given higher doses over a more prolonged period developed the EEG abnormalities

DEMONSTRATIONS

1 Duplicating EEG Recordings — D GORDON (W End Hospital)

An automatic printer for records will be shown consisting of a special printing frame for taking records without cutting or creasing and an automatic timer for exposure

The paper used is Reflex Document Paper giving a white on black trace although black on white traces can be obtained by means of an intermediate negative

2 Inexpensive Electrode Selector — J L COATES (Introduced by M E Heppenstall)

This is designed to give independent connexion of any of 14 electrodes to any amplifier grid by means of telephone jacks and plugs A selected group of electrodes is indicated on an illuminated panel and also on the record itself every 15 seconds

Total cost is less that £4

WESTERN ELECTROENCEPHALOGRAPHIC SOCIETY (U S A)

Officers for 1949 are

President Dr ROBERT S DOW Portland Oregon

Vice President Dr DAVID TALBOT Los Angeles California

Secretary-Treasurer Dr NICHOLAS BERCEL Dept of Electroencephalography Cedars of Lebanon Hospital, Los Angeles 27 California

1 Studies on irradiation of differentiated cerebral excitation and inhibition as indicated by respiration — WILLIAM F ALLEN Department of Anatomy, University of Oregon Medical School, Portland, Oregon

The results of this study are based on thoracic respiratory tracings taken at the time of recording positive and negative foreleg conditioned reflexes after correct conditioned differentiation was obtained from a variety of auditory olfactory general cutaneous and optic analysers Control respiratory tracings before conditioning were as follows Sound and light showed no effect after the first few tests olfactory caused inhibition and general cutaneous demonstrated no change inhibition or excitation

After correct conditioned differentiation was established — *Excitation* of respiration ordinarily occurred during the intervals of correct positive conditioned reflex tests and during an error for a negative conditioned test The amount character and type of excitation varied with the animal and analyser but was consistent for the same test *Inhibition* of respiration usually accompanied correct negative conditioned reflex tests from all excitable and easily inhibited dogs while the neutral type revealed slight or no inhibition but inhibition of respiration accompanied an error for a positive conditioned test A rapid succession of alternate negative and positive conditioned tests demonstrated (1) ability to respond correctly to each and (2) that respiration not only changed correctly but often made the change when in a state of inhibition or excitation A respiratory tracing recorded during a hasty error for a negative conditioned test often exhibits an early excitable phase approximating the foreleg movement which was followed too late by a long pronounced inhibitory wave Likewise correct positive conditioned reflex records may show short intervals of respiratory excitation accompanying two or more foreleg flexions

There are apparently two kinds of cortical excitation and inhibition correct and incorrect

2 Significance of Abnormal EEGs in Disorders of Behavior — MARGARET A KENNARD Department of Surgery, University of Oregon Medical School [1]

According to the data of many observers the per cent of abnormal EEGs in patients in psychiatric hospitals is relatively high and cannot as yet be explained on the basis of any known organic changes About fifty per cent of adult patients with major psychoses or neuroses have abnormal EEGs In children with disorders of behavior the incidence is 60-70% Whereas *in the normal* population the incidence of abnormality is generally said to be about 10% in adults and 12-15% in children

During the past three years on the psychiatric wards of Bellevue Hospital the EEGs of a series of patients between the ages of 5 and 24 have been examined The incidence of abnormal EEGs in this group agreed with the findings of earlier observers Of the 582 patients with no demonstrable organic nervous system disorders there were 65% abnormal

[1] This work was carried out while the author was attached to the Department of Psychiatry on New York University School of Medicine and on the psychiatric wards of Bellevue Hospital

records in patients below the age of 14 Above that age the incidence dropped abruptly to about 50% where it remains throughout the age levels tested Evidence appeared which indicated that sensitivity or reactivity of EEG pattern was the factor most important in producing the dysrhythmic abnormal records There were various influences affecting this sensitivity among which were (1) age of patient (2) familial or inherited tendencies (3) organic insult such as head trauma or infectious processes (4) anxiety or tension states

The total EEG pattern then is a result of all the stabilizing or distorting factors which may have been brought to bear on the cerebral activity

3 Studies in Electronarcosis Therapy Electroencephalographic Investigations — ALEXANDER SIMON, CHARLES L YEAGER and KARL M BOWMAN *The Langley Porter Clinic and The Division* of Psychiatry of the University of California Medical School

Approximately 50 patients receiving electronarcosis therapy were studied by means of the encephalogram An average of 20 treatments were administered to each patient at a frequency of 3 times per week The majority of the patients were schizophrenics but several cases of manic-depressive psychosis and of severe psychoneurosis were included in the group

Electroencephalographic tracings were taken before treatment immediately after an individual treatment, during the course of treatment and for varying periods after cessation of treatment Correlations were made with the clinical condition of the patient The electroencephalographic changes were also compared with those occuring in electro shock therapy

Immediately after the first treatment the electroencephalographic abnormality was mild and persisted no longer than 4 hours but by the end of the fifth treatment when gross abnormalities were noted they failed to diminish from treatment to treatment

It has also been noted that when clonic movements do not occur during the course of treatment the mental condition of the patient does not change However when convulsions are induced the mental state may progressively improve The electroencephalographic changes do not occur in those situations where clonic movements are absent

4 Electroencephalographic Findings in Twenty Six Cases of Verified Subdural Hematomas — A A MARINACCI and H K MARINACCI Los Angeles County Hospital, Los Angeles, Calif

Twenty six cases of subdural hematomas are reported from Dr Carl W Rand s Neurosurgical Service of the Los Angeles County General Hospital An electroencephalogram was taken in all these cases from one to ten weeks after head injury and subsequently subdural hematomas were verified or evacuated surgically

This report is limited to a definite focus of suppressed activity over the hematomas There were twenty-one cases (80%) of unilateral and five cases (20%) of bilateral hematomas In the group of unilateral lesions the electroencephalogram showed a definite focus of suppressed activity consistant with the location of the hematomas In addition the remaining cortical activity was not definitely impaired in seventeen cases but it was greatly impaired in four cases The focal activity varied in the five cases with bilateral lesions In one case with bilateral suppressed foci two large hematomas were evacuated In the remaining four cases there was a focus of suppressed activity over the larger hematoma while on the side of the smaller hematoma the activity varied from moderately suppressed to slow high voltage activity We wish to state that a focus of suppressed activity is not entirely pathognomonic of subdural hematoma

In our experience a focus of suppressed cerebral activity has been found in cases of subdural hematoma severe cerebral contusion large subcortical hematoma hydroma cortical atrophy and porencephalic cyst

5 The Relation of the Permeability of the Blood Brain Barrier to Cerebral Physiology as Reflected by Electroencephalography — ROBERT B AIRD

Cerebral concussion and electric shock therapy when induced experimentally in cats were associated with a marked prolonged increase in the permeability of the blood brain barrier as well as generalized cerebral dysrhythmias of non-specific types as recorded electroencephalographically Preliminary injections of trypan red which previously had been shown by Aird et al to lower the permeability of the blood-brain barrier prevented these changes This suggested that the electroencephalographic changes were dependent upon the permeability of the cerebro vascular system or upon physio chemical factors associated with the permeability of the system Aird points out that the neurogenic mechanisms responsible for the normal electrical rhythms of the brain are dependent upon a normal vascular supply and alterations of the latter may produce changes in the physio-chemical status of the cortex which are reflected in the dysrhythmic activity of a non-specific and usually diffuse form The evidence obtained in these studies would appear to indicate that the dysrhythmias of cerebral concussion and electric therapy are of this type In ad-

dition it is suggested that this same vascular mechanism may explain many of the non-specific dysrhythmias which have been observed electroencephalographically in various other abnormal conditions of the central nervous system

6 The Relationship Between the Bulbar Reticular-Suppressor Region and the EEG — ARTHUR A WARD JR

The pathway from the cortical suppressor areas to the caudate nucleus (over which suppression of electrical activity of the cortex is mediated) is said to be a collateral of the projection to the medial reticular formation of the brain stem Electrical stimulation of the medial reticular formation in anesthetized cats has no effect on the cortical EEG However in the cat paralyzed with beta-erythroidine such brain stem stimulation is followed by a prolonged generalized increase in both the voltage and frequency of the EEG from the entire cortex This striking increase lasts for 40 seconds or longer and is followed by a gradual return to a normal EEG This change has none of the characteristics of after-discharge or of stimulation of afferent tracts The possible relation of this phenomenon to the epileptic activitation obtained during sleep is discussed It is pointed out that the bulbar reticular formation in a sense represents a caudal extension of the midline diffuse circuits which are present in the diencephalon It has already been shown that stimulation at the latter level results in widespread diffuse changes in the cortical EEG which may occasionally resemble petit mal

7 Observations in Electromyography — B FEINSTEIN, E M WEBB, V T INMAN and H J RALSTON

The phasic action of the muscle groups in the lower limb has been studied during various walking activities by means of electromyography

Skin electrodes were placed over the muscles and the action potentials were amplified by means of resistance-capacitance coupled amplifiers Recordings were made with a twelve channel Heiland Oscillograph The complex electromyograph action potentials were simplified by a rectifier-filter device

Eight major muscle groups acting on the lower extremity and pelvis were investigated in ten normal male subjetcs The results were sufficiently constant so that definite patterns of activity could be assigned to the various muscle groups during the different activities

The individual muscles of the lower limb were then examined and their exact phase of action recorded Two wire electrodes were inserted into the belly of the muscle Thus only the activity of that particular muscle was recorded Thin copper wire electrodes insulated to the tip were used These were first threaded through a hypodermic needle and the tip of the wire was hooked over the bevel edge The needle was then inserted into the muscle and the position determined by stimulation The needle was then withdrawn and the hooked wire electrodes remained in place The precise phase of the stride was correlated with the electrical activity of the muscle This was achieved by moving pictures of the various activities synchronized with the electromyographic recordings

There is no relationship between the voltage output of a muscle and its isometric tension except for a given length of muscle These observations were made while studying the length-tension relationships of human voluntary muscle in subjects that had cineplastic muscle tunnels

The electromyographic records of 53 muscles which had been completely dennervated 2 to 3-½ years previously were compared with the power developed by the muscle using an electric strain gauge dynamometer The patients were veterans who had had nerve sutures The results showed a rough general correlation between power and electromyograms but there was sufficient variation so that no useful correlation could be made in individual patients It was shown that valid conclusions as to probable power could not be made from the electromyogram

DANISH EEG SOCIETY

Neurophysiological Institute, Copenhagen, September 30, 1948

TITLES OF COMMUNICATIONS

On the correlation between clinical and electroencephalographic observations in patients treated with electroshock — Poul HONCKE

The EEG of epileptics under CO_2 breathing — Stubbe TEGLBJERG

An account of a journey to England and a visit to the various EEG centers — Hertel WULFF

An account of a journey to the United States and a visit to the various EEG centers

Discussion of the training of EEG personnel

SOCIÉTÉ D'EEG ET DES SCIENCES CONNEXES DE LANGUE FRANÇAISE[1]

DEUXIÈME RÉUNION ANNUELLE

Paris, 8 octobre 1948

1 L'epilepsie induite par la stimulation auditive intermittente rythmee ou epilepsie "psophogenique" — H Gastaut, J Roger, J Corriol et Y Gastaut

Deux malades ont presenté des crises induites par la stimulation auditive intermittente (S A I) alors que 50 en ont presente a la stimulation lumineuse intermittente Le stimulus efficace etait chaque fois un son de hauteur comprise entre 1 et 5 kilocycles interrompu de 8 a 20 fois par seconde

La reponse obtenue etait tantôt a type d absence clinique avec pointe onde paroxystique bilateral synchrone tantot a type de bouffees infra cliniques d ondes hypersynchrones predominant dans les régions temporales et rappelant de tres pres les caracteres d un K complexe surchargé de pointes

La stimulation photo acoustique synchronisee n a pas ete plus active que la stimulation photique

En conclusion 1° La S A I est beaucoup moins efficace que la S L I 2° Elle n est efficace que chez les malades presentant deja les caracteres cliniques et electriques de l epilepsie photogenique 3° De ce fait le mecanisme propose pour cette derniere semble pouvoir lui etre applique 4° Son efficacite moindre semble pouvoir etre rapportee a l importance egalement moindre des voies auditives centrales

2 Étude Electroencephalographique d'un cas d'epilepsie musicogenique — R Hamoir et J Titeca

Il s agit d une femme de 38 ans presentant depuis l âge de 20 ans des crises de grand mal nocturnes associees à des equivalents psycho moteurs declenches par l audition d une musique L audition d un disque de gramophone permet de déclencher 4 crises annoncees au bout de 6 secondes par un malaise épigastrique en meme temps que survient un blocage partiel du rythme alpha A ce moment apparait une déviation de la tete vers la droite et des mouvements stereotypes de grattage pendant que la malade perd conscience et que se developpent sur l EEG des rythmes lents a 6 5 4 et meme 3 c/s de forme a sommet crenele et de voltage superieur a 100 microvolts Duree de la crise une minute puis recuperation progressive de la conscience et du rythme alpha

Les bruits non musicaux les sifflements ne provoquent pas de crises La repétition d une musique qui

1 Epilepsy Induced by Rhythmic, Intermittent, Auditory Stimulation or Epilepsy "Psophogenique" — H Gastaut, J Roger, J Corriol and Y Gastaut

Two patients had attacks induced by intermittent auditory stimulation while there were fifty patients who had attacks with intermittent light stimulation The effective stimulus was in each case a sound with a frequency between one and five kilocycles interrupted eight to twenty times per second

The response obtained was sometimes a form of clinical petit mal or absence with paroxysmal bilaterally synchronous wave and spike discharge or a type of subclinical burst of hypersynchronous waves, most prominent from the temporal region and suggesting very closely the characteristics of a K complex with many spikes A combination of photic and acoustic stimuli synchronized was not more active than photic stimulation alone In conclusion

1 Rhythmic, auditory stimulation is much less effective than rhythmic light stimulation 2 It is effective only in patients presenting already clinical characteristics and electrical characteristics of photogenic epilepsy 3 Because of this fact the mechanism proposed for the latter seems to be applied to the former 4 Its lesser effectiveness seems related to the lesser importance of central auditory pathways

2 Electroencephalographic Study of a Case of Musicogenique Epilepsy — R Hamoir and J Titeca

The patient a woman of 38 years from the age of 20 had attacks of nocturnal grand mal epilepsy associated with psychomotor equivalents which were induced by hearing music Listening to a phonograph record set off four attacks preceded by about six seconds with an epigastric discomfort at the same time as a partial blocking of the alpha rhythm At this time there occurred a turning of the head to the right and stereotyped movements during which the patient lost consciousness and there appeared in the EEG slow rhythms at 6 5 4 and even 3 per second with a notched wave form and a voltage above 100 microvolts The attack lasted one minute followed by progressive recovery of consciousness and the alpha rhythm

Non musical noises such as whistles did not provoke an attack Repetition of a piece of music

---

1 Secrétaire Dr Henri Gastaut 149 Promenade de la Corniche Marseille France

s est averee une premiere fois epileptogene n est plus efficace immediatement apres une crise Il faut a ce moment patienter environ une demi-heure avant de reussir a en declencher une nouvelle

3 Action de l'insuline intra veineuse sur l'EEG de quelques traumatises anciens du crâne — A Baisset, L Bugnard, Ch et F A Grezes Rueff et J Planques

Application de l epreuve de l hypoglycemie provoquee par insuline intra-veineuse (une unite par 3 kg de poids) a 16 traumatises anciens du crane porteurs de sequelles diverses en particulier d un syndrome subjectif

L EEG de tous ces sujets etait normal même apres hyperpnee Chez 7 d entre eux l insuline intra veineuse a fait apparaitre sur le trace des anomalies diverses

4 Detection bio electrique d'une tumeur cerebrale sous corticale par l'EEG active (cardiazol) et l'ECG — J Paillas, H Gastaut et J Duplay

Sujet adulte mâle presentant des crises jaksoniennes gauches sans signes d hypertension intra-crânienne

EEG standard normal EEG active par l injection intra-veineuse de 2 cc de cardiazol mettant en evidence un foyer particulierement net d ondes delta polyrythmiques obtenues en opposition de phase sur une etendue tres limitee de la region parieto occipitale droite

La ventriculographie montre des anomalies difficilement interpretables du ventricule droit

La crâniotomie dirigee sur le foyer électrique decouvre un cortex parfaitement normal sur lequel l ECG permet de retrouver en l absence de toute activation, un foyer d anomalies de siege et de forme correspondant a celui decele pendant l EEG active La ponction au-dessous du foyer rencontre une tumeur sous-corticale arrivant jusqu a 3 cm du cortex Exerese neuro-chirurgicale

L activation au cardiazol ne vaut donc pas que pour les lesions epileptogenes corticales mais aussi pour les foyers tumoraux même sous-corticaux

5 Note preliminaire sur les resultats fournis par l'electrographie directe des lobes occipitaux de l'homme pendant la stimulation lumineuse intermittente — H Gastaut et J Duplay

Exploration a l aide d aiguilles-electrodes bipolaires introduite par des trous de ventriculographie de l activite des lobes occipitaux depuis le cortex jusqu aux ventricules La comparaison des flickers ainsi obtenus avec ceux recueillis sur le scalp montre

which had induced a seizure the first time is no longer effective immediately following a seizure It is necessary to wait about one-half hour after an attack before a new one can be provoked

3 The Action of Intravenous Insulin on the EEG of Patients with Old Head Injuries — A Baisset, L Bugnard, Ch and F A Grezes Rueff and J Planques

Results are presented from the application of the hypoglycemic test induced by intravenous insulin (one unit per 3 kilograms body weight) to 16 patients with old head injuries and with various symptoms in particular, those of a subjective character The EEG in all these subjects was normal but after hyperventilation in seven of them with intravenous insulin there appeared diverse abnormalities in the records

4 The Bio Electric Detection of a Subcortical Tumor by Means of the EEG Activated by Cardiazol and the ECG — J Paillas, H Gastaut and J Duplay

The subject was an adult male presenting Jacksonian attacks of the left side without signs of intracranial hypertension The usual EEG was normal Following the injection of 2cc of cardiazol there appeared in the EEG a focus particularly clear with polyrhythmic delta waves showing a phase reversal localization over a very limited region of the right parieto-occipital area The ventriculogram showed some anomalies of the right ventricle which were difficult to interpret

The craniotomy directed towards the electrographic focus revealed the cortex to be perfectly normal but an electrocorticogram made it possible to find again the focus corresponding to that obtained pre operatively by the activated EEG Puncture beneath this focus lead to a subcortical tumor which reached just three centimeters below the cortex It was removed

Activation by cardiazol is not only effective for cortical epileptogenic lesions but also for focal neoplastic lesions even those beneath the cortex

5 A Preliminary Note on the Results Obtained by Direct Electrographic Recording from the Occipital Lobe in Man During Intermittent Light Stimulation — H Gastaut and J Duplay

Bipolar recording electrodes were introduced through ventriculograph burr holes and the activity of the occipital lobes was recorded Comparison of the flicker responses thus obtained with those obtained on the scalp showed considerable advantage to this

les avantages considerables de cette nouvelle methode appreciation de la forme de l amplitude et de la phase de la réponse a differentes profondeurs sans l interference de l activite de toute une population neuronique qui realise des phenomenes de masquage

Presentation de nombreux exemples des resultats obtenus permettant des constatations surprenantes sur la signification generale du processus

6 Correlation entre le taux glycemique et le trace EEG — LUQUET et Y PARRAT

Distinction de trois categories de cas

1 — *Hypoglycemie spontanee absolue ou relative*

a) *hypoglycemie spontanee pure par adenome du pancreas hyperinsulinemie ou hyperadrenalinemie* La symptomatologie est variable l hypoglycémie a jeun franche le trace normal des que la glycemie est rendue normale par ingestion de sucre les anomalies a l hyperpnee disparues des que la glycemie est superieure a 1 gr 20

b) *Epilepsie hypoglycemique* La glycemie a jeun est abaissee le trace partiellement normalise lorsque la glycemie est rendue normale les anomalies a l hyperpnee persistent souvent lorsque la glycemie est superieure a 1 gr 40

c) *Epilepsie avec hypoglycemie relative* La glycemie a jeun est normale le trace amelioré lorsqu une hyperglycemie est provoquée par ingestion de sucre Ces malades doivent donc etre traites en plus des anti convulsivants habituels par l absorption de sucre meme lorsque leur glycemie est normale

2 — Hypoglycemie provoquee (cure de Sackel)

3 — Hyperglycémie provoquée

Diabetiques epileptiques ou non soumis au traitement insulinique Tout se passe comme si le diabete et l epilepsie etaient des maladies antagonistes le 1er corriegeant en partie les manifestations de la seconde

7 Activation de l EEG par le pentothal — G HEUYERE, A REMOND et R DELARUE.

L injection intra-veineuse d une petite dose de pentothal entraine sur les traces deux types de reactions I) reaction rapide constituee par un rythme rapide ample et regulier predominant sur la moitie anterieure de l encephale II) reaction lente constituee par un rythme lent et ample ou de grandes ondes lentes isolees

Chacune de ces deux modifications peuvent etre isolees mais elles sont plus souvent intriquees donnant eventuellement au trace l apparence plus ou moins suggestive d une serie de pointe-ondes Dans

new method appreciation of the form the amplitude and the phase of the response at different depths in the cortex without interference from activity derived from an entire population of neurones which causes phenomena of masking Presentation of numerous examples of results obtained make possible surprising conclusions regarding the general significance of this process

6 Correlation Between Blood Sugar Level and the EEG Record — LUQUET and Y PARRAT

Distinction is made between three categories of patients

1 *Spontaneous hypoglycemia absolute or relative*

(a) *Pure spontaneous hypoglycemia due to adenoma of the pancreas hyper-insulinemia or hyper-adrenalinemia* The symptomatology is variable When hypoglycemia is due solely to the fasting state the EEG becomes normal as soon as glycemia is rendered normal after ingestion of glucose Then the abnormalities recorded during hyperventilation disappear as soon as the glycemic state is over 120 mg per cent

(b) *Hypoglycemic epilepsy* Normally glycemia is lowered when fasting and the EEG becomes partially normal when glycemia is rendered normal Abnormalities seen during hyperventilation often persist when glycemia is over 140 mg per cent

(c) *Epilepsy with relative hypoglycemia* When glycemia is normal when fasting the EEG is improved with ingestion of glucose to induce hyperglycemia These patients should then be treated with glucose ingestion besides the usual anti-convulsive drugs even if their glycemia is normal

2 *Induced hypoglycemia* (Sackel therapy)

3 *Induced hyperglycemia*

Diabetic patients whether epileptic or not under insulin treatment One may consider diabetes mellitus and epilepsy to be antagonistic diseases the former disease partially improving the clinical manifestations of the latter

7 Activation of the EEG by Pentothal — G HEUYERE, A RÉMOND and R DELARUE

The intravenous injection of a small dose of pentothal produces two different types of reactions on the record 1 A rapid reaction composed of a fast large and regular rhythm predominating from the anterior half of the cerebrum 2 A slow reaction made up of a slow and large rhythm or of large and slow isolated waves

Each of these alterations may be isolated but most often they are integrated eventually giving the tracing the appearance more or less suggestive of a series of spikes and wave forms In certain cases

certains cas ce dernier aspect est suffisamment caractéristique pour permettre d'affirmer l'existence d'un mécanisme électrique de type épileptique

8 Rythmes EEG et lésions anatomiques dans 20 cas de tumeurs temporales — O R CARVALHO

Anatomiquement il s'agissait de 7 glioblastomes multiples une métastase d'épithélioma 4 astrocytomes 6 méningiomes un cholestéatome et un hématome intra-cérébral

Électriquement on trouvait 3 types d'altérations I) SILENCE ÉLECTRIQUE avec oscillations lentes et irrégulières de la ligne de base et suppression de l'alpha II) ONDES LENTES POLYRYTHMIQUES et irrégulières III) ACTIVITÉ LENTE monorythmique et harmonique De tous ces signes c'est le silence électrique qui s'est révélé être le facteur de localisation le plus fidèle et le plus direct tandis que les anomalies lentes et irrégulières ne constituent que des signes de voisinage et l'activité lente un signe transmis à distance

9 Valeur pronostique de l'EEG dans les tumeurs de la fosse postérieure — M BOHM

Les tracés peu altérés ou normaux accompagnent d'habitude les tumeurs bénignes à évolution lente l'issue opératoire est favorable dans 64% des cas Les tracés modérément altérés accompagnent des tumeurs presque toujours malignes et à évolution rapide l'issue favorable n'est plus rencontrée que dans 27% des cas Les tracés très perturbés s'accompagnent de mortalité dans 100% des cas

Les rythmes lents généralisés de 4 à 7 sont visibles dans les tumeurs du tronc cérébral tandis que les tumeurs des hémisphères cérébelleux altèrent surtout le rythme des régions frontales

10 Épreuve de l'hyperpnée et dérivation basale — J FAURE, H JASPER et L HENDERSON

Le tracé basal obtenu par l'électrode nasale réagit à l'hyperpnée comme le tracé cortical Une dérivation spéciale reliant l'électrode auriculaire à l'électrode temporale et celle-ci à l'électrode basale permet de bien mettre en valeur l'effet de l'hyperpnée sur la base du cerveau En outre cette dérivation a l'avantage I) d'établir une comparaison entre les potentiels captés par l'électrode auriculaire et ceux captés par l'électrode basale II) d'enregistrer les foyers situés dans les parties profondes du lobe temporal près de la ligne médiane

11 Contribution à l'EEG de l'anxiété — J FAURE

Présentation de tracés ou chez les anxieux le

this latter appearance is sufficiently characteristic to show an electrical mechanism of an epileptic type

8 EEG Rhythms and Anatomical Lesions in 20 cases of Temporal Lobe Tumor — O R CARVALHO

There were 7 glioblastomas multiforme one metastatic epithelioma 4 astrocytomas 6 meningiomas, 1 cholesteatoma and one intracerebral hematoma

Electrically, three types of alterations were found 1 *Electrical silence* with slow and irregular oscillations of the base line and suppression of the alpha rhythm 2 *Slow polyrhythmic* and irregular waves, 3 *Slow activity* monorhythmic and harmonic Of all these signs electrical silence was the most trustworthy and the most direct while the slow and irregular anomalies constituted signs of adjacent areas and slow rhythmic activity was a sign transmitted at a distance

9 Prognostic Value of the EEG in Tumors of the Posterior Fossa — M BOHM

Normal or slightly changed tracings are usually seen with non-malignant tumors of slow growth Operation is successful in 64 % of cases Moderately altered tracings are encountered nearly always with malignant tumors of rapid growth operation is successful in but 27% of cases There was 100% mortality in patients with severely abnormal records

Slow generalized rhythms of 4 to 7 per second are found in tumors of the brain stem while tumors of the cerebral hemispheres alter mostly the rhythm of the frontal regions

10 Hyperpnea and the Basal Derivation — J FAURE, H JASPER and L HENDERSON

The basal tracing derived from the nasal electrode reacts to hyperpnea just as the cortical tracing does A special derivation joining the auricular electrode to the temporal electrode and the latter to the basal electrode shows markedly well the effect of hyperpnea on the base of the cerebrum Besides, this derivation has the following advantages 1 Comparison possible between the potentials at the auricular electrode and those at the basal electrode 2 Registration of foci deeply seated in the temporal lobe near the median line

11 Contribution to the EEG in Anxiety — J FAURE

Presentation of tracings of anxiety patients in

rythme alpha est remplacé d'une part par un rythme theta et d'autre part par un rythme beta

12 Les formes EMG de la tetanie — R TURPIN, J LEFEBVRE, J LERIQUE et P DORLAND

A côte de la forme tonique caracterise par le doublet les auteurs insistent sur la forme fibrillaire decrite par KUFFLER

13 Oscillographie de l'epilepsie corticale faradique et strychnique chez le chat — GUY NOËL

L'excitation faradique de l'ecorce du chat a encéphale isole entraine des modifications variables suivant l'intensite du stimulus pour de faibles intensités simple intensification de l'activité normale pour une intensite plus grande depression marquee pour des intensites elevees after discharge synchrone et généralisee caracterisant la crise epileptique

La durée des crises est egalement fonction de l'intensite mais aussi de la frequence et de la duree du stimulus

La perturbation epileptique une fois declenchee tend a se propager et a envahir les regions voisines

Deux foyers faradique et strychnique reagissent reciproquement l'un sur l'autre

14 Effet du curare sur la transmission synaptique de la moelle epiniere chez le chien spinal — A BAISSET, YVES LAPORTE et F GREZES RUEFF

La d-tubocurarine n'a pas d'action sur la transmission synaptique de la moelle epiniere chez le chien spinal

La d-tubocurarine ne retentit sur la transmission medullaire qu'a travers le collapsus vasculaire qu'elle est susceptible de provoquer lors de son injection intra veineuse rapide

15 ECG de l'epilepsie provoquee par electro choc chez le rat curarise non anesthesie — H GASTAUT, J CORRIOL, J CAIN et J MERCIER

Presentation d'une abondante iconographie concernant 62 crises entierement enregistrees sans interference de myogramme ni de mecanogramme du fait de la curarisation des animaux Signification particuliere des documents enregistres chez l'animal non anesthesie a metabolisme cortical non modifie

59 traces sur 62 sont pratiquement superposables et repondent a une crise type qui est analysee

16 Le probleme des analyseurs de frequence en EEG — G MINOT

Multiplicateur de frequences de coefficient 40 base sur un procedé original photoelectrique Ceci permet l'analyse a l'aide des moyens classiques d'enregis-

which the alpha rhythm is replaced on one hand by a theta rhythm and on the other hand by a beta rhythm

12 Forms of EMG in Tetany — R TURPIN, J LEFEBVRE, J LÉRIQUE and P DORLAND

Besides the tonic form characterized by the doublet the authors have emphasized the fibrillary form described by Kuffler

13 Oscillography of Cortical Epilepsy Following Faradic Stimulation and Strychnine in the cat — GUY NOËL

The faradic stimulation of the cortex of a cat with an isolated encephalon causes modifications varying with the intensity of the stimulus with weak intensities simple intensification of normal activity with stronger intensities marked depression with still stronger intensities synchronous and generalized afterdischarge characteristic of an epileptic seizure

The duration of the seizures is proportional not only to the intensity but also to the frequency and the duration of the stimulus Once started the epileptic perturbation tends to invade the adjoining regions Two foci faradic and strychninized tend to react reciprocally one upon the other

14 Effects of Curare on Synaptic Transmission of the Spinal Cord in a Spinal Dog — A BAISSET, YVES LAPORTE and F GREZES RUEFF

Subocuraine has no effect on the synaptic transmission of the spinal cord in the spinal dog

It may act on spinal transmission only through a vascular collapse which may be caused by its rapid intravenous injection

15 ECG of Epilepsy Induced by Electroshock in a Curarized but not Anaesthetized Rat — H GASTAUT, J CORRIOL, J CAIN and J MERCIER

Presentation of an abundant iconography of 62 seizures completely recorded without interference of myogram or mechanogram due to curarization of the animals

Of particular significance were the records from unaesthetized animals with cortical metabolism unmodified

59 tracings out of 62 are practically superposable corresponding to a typical seizure which is analyzed

16 The Problem of Frequency Analyzers in EEG — G MINOT

A multiplier of frequencies with a coefficient 40 based on an original photoelectrical process is described This permits the analysis with the aid of

trement du spectre des frequences ainsi qu a l aide de casques et de haut-parleur realisant une veritable auscultation cerebrale

the classical means of registration of the spectrum of frequencies and also with the aid of helmets and of a loudspeaker making possible a veritable cerebral auscultation

CENTRAL ASSOCIATION OF ELECTROENCEPHALOGRAPHERS

Chicago, November 27-28, 1948

TITLES OF COMMUNICATIONS

The Basis of Analysis of the Electroencephalogram — F F OFFNER, Offner Electronics, Inc , Chicago, Ill

Pathways of Electrical Current in the Brain — F M LORIMER, M M SIEGEL and S N STEIN, University of Ill Med School

Subcortical Centers as Pacemakers of Cortical Activity — E GELLHORN, University of Minnesota Medical School

"Feedback" Effects Related to Autonomic Changes — C W DARROW, Institute for Juvenile Research, Chicago, Ill

Electroencephalogram During a Cycle of Addiction to Keto Bemidone Hydrochloride — S ALTSHUL and A WIKLER, U S Public Health Service Hospital, Lexington, Ky

A Preliminary Report on the Somatic Afferent and Auditory Areas of the Cerebral Cortex of the Marmoset — Clinton WOOLSEY, Department of Physiology, Service Memorial Institutes, University of Wisconsin

Arousal Response During Sleep as a Test of Sensory Function — R E MARCUS, E L GIBBS, and F A GIBBS, University of Illinois Medical School

The Electroencephalogram in Chronic Alcoholism — W H FUNDERBURK, Traverse City State Hospital, Traverse City, Michigan

Electroencephalographic and Metabolic Studies Before and After Frontal Lobotomy — R ROSSEN, N BRADLEY, R SCHROEDER, and A REICHENBERG, Hastings State Hospital, Hastings, Minnesota

EEG Findings in Hypertension and Their Correlation with the Clinical Status, Operative Risk and Post operative Confusion — B K BAGCHI, K A KOOI, and S W HOOBLER, The Neuropsychiatric Institute, University of Michigan

Findings in Thirty Five Head Injuries with Surgically Verified Brain Damage — Dr E C CLARK, Henry Ford Hospital, Detroit

A Preliminary Report on Therapeutic Results of Temporal Lobotomy for Psychomotor Epilepsy — Percival BAILEY and F A GIBBS

ABSTRACT

Electroencephalographic and Clinical Responses to Light Stimulation in Normal Subjects — R G BICKFORD

The electro-encephalographic and clinical responses to light stimulation produced by a strobolux discharge tube and by sectored light have been investigated in 50 normal subjects Their ages ranged from four to twenty-seven years The resting electroencephalographic records of 14 per cent were classified as abnormal

The electrical responses to light stimulation may be divided into three categories (1) direct driving response which appears at the flash frequency or a multiple or submultiple of it and is usually confined to the occipital and parietal areas (2) slow complex delta discharges confined to the occipital and parietal areas but unrelated to the flash frequency and (3) generalized paroxysmal discharges usually synchronous over the whole cortex and not directly related to flash frequency Light stimulation induced one or more of the above responses in 92 per cent of the group and had not appreciable effect on the cortical potentials in the remaining 8 per cent The driving response (type 1) was present in 92 per cent of subjects the amplitude being greater in the older age groups It was associated with subjective sensations of light and color which were not often unpleasant

The delta discharges (type 2) were present in 10 per cent of the subjects They were usually associated with unpleasant feelings of dizziness and disorientation and in 1 case their appearance preceded a clinical seizure

Paroxysmal discharges (type 3) were present in 14 per cent of the subjects Clinical seizures were induced in 2 subjects showing this type of discharge In the remaining 5 subjects of this group a variety of unpleasant subjective effects were noted

The strobolux light was slightly more effective in producing the driving response (type 1) than was the sectored light Discharges of types 2 and 3 were more frequently produced by the sectored light Clinical seizures were produced only by sectored light

ANNOUNCEMENTS

DEUXIÈME CONGRÈS INTERNATIONAL D'ÉLECTROENCÉPHALOGRAPHIE

Paris 1, 2, 3 septembre 1949

Comite d'organisation du Congres

President du Congres A Baudouin (France)
Vice-President F Bremer (Belgique)
Membres du Comite
Amerique Latine J Odoriz
Canada H Jasper
Chine
Danemark H Herz
États Unis F A Gibbs et R Schwab
Grande Bretagne W Grey Walter et D Hill
Hollande J ten Cate
Italie M Gozzano et G Morruzi
Mexique A Rosenblueth
Roumanie A Kreindler
Suede T S Frey Jr
Suisse M Monnier
Tchecoslovaquie K. Henner
Turquie F K Gokay
URSS

Secretaire general H Fishgold
Secretaire H Gastaut
Secretaire A Remond
Tresorier G Verdeaux

Date du Congres

Le Congres International d EEG se tiendra a Paris les 1er 2 et 3 septembre 1949 Un jour de la semaine suivante sera occupe par une seance commune des Congres Internationaux de Neurologie et d Electro encèphalographie

Le choix des locaux sera fait ulterieurement par le Comite d organisation

Rapports

A la suite des suggestions faites par les Comites des differentes societes nationales d EEG le pro gramme des rapports a ete ainsi etabli

1° Le Jeudi 1er septembre a 9h 30 W GREY WALTER Principes et methodes de localisation
de 10 a 11h Discussion du rapport
a 14h 30 F A GIBBS Enregistrement direct chez l homme des structures corticales et sous corticales
de 15 a 16h Discussion du rapport

2° Le Vendredi 2 septembre a 9h H BRAZIER Les champs electriques cerébraux et leurs effets
de 9h 30 a 10h 30 Discussion du rapport

3° Le Samedi 3 septembre a 9h H GASTAUT et V J WALTER Effets des stimulations physiques sur l EEG
de 9h 30 a 10h 30 Discussion du rapport
a 14h 30 A REMOND Y LAPORTE et C BRISSAC Effets des stimulations chimiques sur l EEG
de 15h a 16h Discussion du rapport

4° Pour la journee commune des Congres Internationaux de Neurologie et d Electroencephalographie
F BREMER Bases physiologiques de l EEG
H JASPER EEG in neurosurgical diagnosis
F A GIBBS EEG in neurological diagnosis
F BUCHTAL Electromyography in neurological diagnosis (central nervous disease)
M HARVEY Electromyography in neurological diagnosis (peripheral nervous disease)

La discussion sera libre mais ne pourra depasser 3 minutes exception faite pour les orateurs inscrits a l avance auxquels seront accordees 5 minutes

A la suite de la discussion du rapport chaque seance sera consacree a des communications diverses

Les textes des rapports doivent etre adresses au plus tard le 1er mars au Dr FISCHGOLD Librairie MASSON & Cie 120 bd Saint Germain a Paris (6°)

Communications

Elles devront etre adressees
pour l Amerique au Dr R SCHWAB
Massachussetts General Hospital
BOSTON 14 (Mass) U S A
pour l Europe au Dr REMOND
131 Boulevard Malesherbes
PARIS (17°)

qui les soumettront aux Comites de coordination etablis pour chacun des Continents

Le dernier delai auquel le titre et le resume des communications (500 mots au plus) pourront etre remis aux Secretaires susnommes des Comites de coordination est fixe au 1er mai 1949

Inscriptions

Toute personne s interessant a l Electroencephalographie peut se faire inscrire en tant que Membre titulaire en s adressant aux Secretaires des Comites de coordination dont elle depend (Dr SCHWAB pour l Amérique Dr REMOND pour l Europe)

Les personnes s interessant au Congres peuvent être nommées membres associes

Afin de couvrir les depenses de l organisation du Congres chaque membre titulaire versera une somme de 10 dollars ou son equivalent, cette cotisation donnera droit a l envoi du texte imprime des rapports, discussions et communications du Congres International d Electroencephalographie

Chaque membre associe devra verser la somme de 5 dollars ou son equivalent

La liste des membres sera close le 1er mai 1949

Reception des Congressistes

Un Comite de reception siegera avant et pendant le Congres et se tiendra a la disposition des Congressistes

Pour tous renseignements complementaires s adresser au membre du Comite representant les U S A Dr R Schwab Massachusetts General Hospital Boston 14 (Mass) U S A

ou au Secretaire pour l Etranger de la Societe d Electroencephalographie de Langue Française Dr H Gastaut 149 Promenade de la Corniche a Marseille

SECOND INTERNATIONAL EEG CONGRESS

Paris, September 1, 2, 3, 1949

Organization Committee of the Congress

President of Congress A Baudouin (France)

Vice-President F Bremer (Belgium)

Members of the Committee

Latin America J Odoriz
Canada H Jasper
China
Denmark H Herz
United States F A Gibbs and R Schwab
Great Britain W Grey Walter and D Hill
Holland J Ten Cate
Italy M Gozzano and G Morruzi
Mexico A Rosenblueth
Roumania A Kreindler
Sweden T S Frey Jr
Switzerland M Monnier
Turkey F K Gokay
Czekoslovakia K Henner
U S S R

Secretary General H Fishgold

Secretary H Gastaut

Secretary A Remond

Treasurer G Verdeaux

Date of Congress

The committee on organization of the Second International EEG Congress is given above The dates given Sept 1-3 1949 are on Thursday Friday and Saturday of the week preceeding the International Neurological Congress One day of the following week will be devoted to a combined meeting of the EEG and Neurological Congress This will consist of a symposium on Electroencephalography and Electromyography

Reports

Following suggestions derived from the various national EEG Societies the following general program has been established

Thursday Sept 1 9 30 A M

Principles and methods of localization W Grey Walter

Discussion, 10 to 11 A M

2 30 P M

Direct Recording from Cortical and Sub-cortical Structures in Man Frederic A Gibbs

Discussion 3 to 4 P M

Friday Sept 2 9 00 A M

Electrical fields at the surface of the head their distribution in various conditions Mary A B Brazier

Afternoon session to be arranged

Saturday Sept 3 9 00 A M

Effects of physical stimuli upon the EEG H Gastaut and Vivian J Walter

Discussion 9 30 to 10 30 A M

2 30 P M

Effects of chemical stimuli upon the EEG A Remond, Y Laporte and C Brissac

Discussion 3 to 4 P M

Combined meeting with the Neurological Congress

Physiological Bases of the EEG F Bremer
The EEG in Neurosurgical Diagnosis H Jasper
The EEG in Neurological Diagnosis F A Gibbs
Electromyography in Neurological Diagnosis (diseases of the CNS) F Buchtal
Electromyography in Neurological Diagnosis (peripheral neuromuscular diseases) M Harvey

Discussion will be open but limited to 3 minutes except for prearranged speakers who will be allowed 5 minutes

Following the discussion of each of the above principal papers individual communications will be presented

Manuscripts of the principal reports should be sent by March 1st 1949 to Dr H Fischgold Librairie Masson et Cie 120 Bd St Germain Paris (6e)

Communications

American to Dr R S Schwab
Massachusetts General Hospital
Boston 14 Mass USA

European to Dr A Remond
131 Boulevard Malesherbes
Paris (17e) France

who will submit them to coordinating committees for their respective continental areas

Abstracts not exceeding 500 words must be received by the above secretaries not later than May 1 1949

Registration

Everyone interested in Electroencephalography may register by writing to one of the above secretaries of the Coordinating Committees

In order to cover the expenses of organizing the Congress each titular member shall pay a fee of ten dollars ($10 US) or its equivalent this fee covering the cost of the printed proceedings of all papers communications and discussions of the International Congress of Electroencephalography Associate members (who will not receive the printed proceedings) may register with a fee of five dollars ($5 00)

Membership will be closed on May 1st 1949

Reception

A reception committee will be at the disposition of the members of the Congress before and after the Scientific Sessions

Information not provided in this announcement may be obtained from Dr R S Schwab Mass Gen Hospital Boston 14 Mass USA or from Dr H Gastaut 149 Promenade de la Corniche Marseille France

THE AMERICAN EEG SOCIETY

ANNUAL MEETING

Atlantic City, June 11 12, 1949

Communications Saturday June 11
Symposium on *Thalamo Cortical Mechanisms*
with the American League Against Epilepsy Sunday June 12

NEW SOCIETIES

SOUTHERN SOCIETY OF ELECTROENCEPHALOGRAPHY

We are pleased to announce the establishment of the Southern Society of Electroencephalography in the United States The first annual meeting was held in Dallas Texas December 5 1948 The officers are President Martin L Towler MD Galveston Vice-President Richard L Masland MD Winston Salem and Secretary-Treasurer Samuel C Little MD, 2111 Highland Ave Birmingham Alabama USA

GROUPEMENT SUISSE D'ÉLECTROENCÉPHALOGRAPHIE

We are pleased to announce the foundation of a Groupement Suisse d Electroencephalographie The Swiss society has been recently organized with the following officers

President Prof Oscar Wyss Ecole de Medecine Geneva Switzerland

Secretary Dr R Hess Heliosstrasse 22 Zürich Switzerland

To the Swiss Society your colleagues throughout the world send best wishes

COMMENTARY

To our Japanese colleagues we extend our sincere regrets and sympathy in the loss of Professor Dr Yasuji Kakegawa of the Niigata Medical College who died on November 13 1948 As a tribute to Professor Kakegawa who has been a leader in developing electroencephalography and neurophysiological research in Japan following the war we quote the following letter from his associate Professor Masaichi Sawa who gives an interesting account of the development of electroencephalography in Japan

Dear Professor Jasper

It grieves me that this first letter to you whom I so deeply respect should be a bad report about Professor Yasuji Kakegawa my senior and excellent collaborator

Professor Kakegawa passed away on November 13th leaving behind him an outstanding achievement in electroencephalographic study of Japan To his last moment he kept his passion for his study making effort to compile the result of his research His great hope was that he may be enabled by your kindness to attend the international meeting at Paris next year As I report to you of his death I here express my deep gratitude to you for your friendship with him

Now since you refer to EEG in Japan in your letter I feel responsible of writing you though briefly about the present state of progress of EEG in Japan Probably EEG research in Japan was opened up by Professor Katsunuma in about 1936 under the instruction of Professor Kornmuller of Germany

Later on Ito Kaketa Professors Motokawa and Kakegawa continued their earnest study of it even since before the war but it did not make a progress notable enough to attract general attention the work being rather elementary Particularly during the war this research work as other scientific researches suffered from much difficulty In spite of this handicap Professors Motokawa and Kakegawa s work constantly presented fine results In particular Professor Motokawa s theoretical study concerning the origin of brain wave though it has some evident defects detectable even by us is worth introducing to you brain wave scholars of both England and America for your investigation and criticism Those articles were submitted to the Tohoku Journal of Experimental Medicine So as I write you this letter I also am going to ask Professor Motokawa to send those articles to you

After the termination of the war quite a number of students of brain waves have appeared which I think is an evidence of great improvement in general interest in this line of study They have formed a special group for brain-wave research in the medical section of Japan Scientific Research Council and keeping a close contact with each other they are doing earnest research However the impoverished financial state of post war Japan which has hampered every progressive effort in the country has retarded our progress also

One of the general tendencies of the post war research is the theoretical inquiry about this Motokawa s theory of brain wave origin which is being undertaken chiefly by Professor Imabori the Institute of Applied Electricity of Hokkaido University Sapporo and Professor Sato of the Department of Physiology Niigata Medical College The other is clinical application which is being attempted in a number of medical institutions but which I am afraid is by far inferior to yours due to our technical and financial poverty The technical efficiency may be improved in the future since the cooperation by electrical engineering has become quite active but one of the important factors for our future development will be the cooperation and assistance of advanced nations in reference to the amplifying and recording apparatus

We now keenly wish to have some one of our group attend the international meeting at Paris now that Professor Kakegawa has been lost we hope some one will take his place in this privilege for the attendance will mean so much to us in getting the information and knowledge as to how other countries have been working on their EEG problems during and after the war and at the same time it will give us a good opportunity to show them what we entirely cut off from the other part of the world have been doing

With many thanks for you

Most sincerely yours

(signed) Masaichi SAWA M D
Professor of Special Course of Medicine
Department of Neurology and Psychiatry
Niigata Medical College Niigata Japan

Reprints enclosed

KAKEGAWA Y Electroencephalographic Study of Narcosis and Sleep *Acta Medica Hokkaidonensia* 1944 22 56 74

KAKEGAWA Y Electroencephalographical Changes during Mental Efforts *Folia Psychiat et Neurol Japonica* 1947 2 109 123

KAKEGAWA Y A new Method for continuous Oscillographic Recording of Cerebral Blood Flow *Folia Psychiat et Neurol Japonica* 1947 2 156-164

KAKEGAWA Y SAWA M and HORIUCHI K Cerebral Blood Flow and Electrical Corticogram preceding and during Cardiazol Convulsion in Man and Cat *Folia Psychiat et Neurol Japonica* 1947 2 249-260

SAWA M Spontaneous electrical Activities obtained from Human Spinal Cord *Folia Psychiat et Neurol Japonica* 1947 2 156 179

SAWA M Functional Interrelation of Cerebral Hemispheres Mediated by Corpus Callosum in Cat *Folia Psychiat et Neurol Japonica*, 1947 2 221-248

KAMBARA H and SAWA M A case of Identical Twins with Little s Disease *Folia Psychiat et Neurol Japonica* 1947 2 369 378

INDEX TO LITERATURE

Edited by Charles Henry

MARGARIA R The rhythm of activity of motor neurones an interpretative hypothesis of the electroencephalogram *Arch neerl physiol* 1948 *28* 399-407

MARSAN C A & FUORTES M G F Elettroencefalografia scopi possibilita e metodi *Arch psicol neur* Milano 1948 *9* 260-287

MAURO A & BLACK S P W An electronic controller of volleys in electrical stimulation *Yale J Biol & M* 1948 *20* 567-569

MEYER A & MCLARDY T Posterior cuts in prefrontal leucotomy a clinicopathological study *J Ment Sc* Lond, 1948 *94* 555-564

NEFF W D & YELA M Function of the auditory cortex the localization of sound in space *Am Psychol* 1948 *3* 243

NOELL W K The recovery of the brain from anoxia after administration of analeptic drugs electroencephalographic studies on rabbits *J Aviat M* 1948 *19* 337-345

NOELL W K & CHINN H I The cerebral survival time of rabbits in anoxia *School of Aviation Medicine* Randolph Field Texas *Quarterly Research Report* Oct 1948 Project #21-02-071 5-6

O LEARY J L Guide to the indications for brain wave recording *Dis Nerv Syst* 1948 9 263-269

PICK E P & FEITELBERG S Thermogenetic action of adrenalin and benzedrine on the brain *Arch internat pharm dyn* Gand 1948 *77* 219-225

PRAST J W & NOELL W K Anoxia warning device I The slow wave activity of the brain during earlier stages of oxygen lack *School of Aviation Medicine* Randolph Field Texas *Quarterly Research Report* Oct 1948 Project #21-02-050 4-5

REITMAN F Evaluation of leucotomy results *Am J Psychiat* 1948 *105* 86-89

RENSHAW B & ROSENBAUM H Respiratory pathways in the cervical spinal cord *Anat Rec* 1948 *101* 738

RICARD A & GIRARD P F De la leucotomie prefrontale unilaterale gauche au probleme des dominances cerebrales les diphrenies *Lyon chir* 1948 *43* 526 531

RICCIUTI H N A comparison of critical flicker frequency n psychotics psychoneurotics and normals *Am Psychol* 1948 *3* 276 277

ROTHERAM W An electronic method for immediate visual recording of the pulse rate *Brit J Phys M*, 1948 *11* 115

ROWLAND L P & METTLER F A Relation between the coronal suture and cerebrum *J Comp Neur* 1948 *89* 21-40

RUSSELL R W PIERCE J F (et al) A new apparatus for the controlled administration of electroconvulsive shock *J Psychol Provincetown* 1948 *26* 71-82

SARNOFF S J HARDENBERGH E & WHITTENBERGER J L Electrophrenic respiration *Science* 1948 *108* 482

SCHIFF E DUGAN P KENNARD M A & WELCH L Effects of pathological anxiety in childhood on EEG and conditioned PGR *Am Psychol* 1948 *3* 371

SCHNEIDER G L electroencephalographie *Schweiz Bl Krankenpfl* 1948 *41* 192

SCIAPONI G H Reversal of circulation of the brain partial reversal in four humans treated for paralysis and mental conditions *Am J Surg* 1948 *76* 150-164

SHANES A M & HOPKINS H S Effect of potassium on resting potential and respiration of crab nerve *J Neurophysiol* 1948 *11* 331-342

SPEIDEL C C Growth of nerve fibers as revealed by fast motion cine-photomicrography *Anat Rec* 1948 *101* 697

SPIEGEL, E A Progress in neurology and psychiatry an annual review New York Grune Stratton 1948 *14* 661 pp

SZENTAGOTHAI J Anatomical considerations of monosynaptic reflex arcs *J Neurophysiol* 1948 *11* 445 454

TASAKI I & FUJITA M Action currents of single nerve fibers as modified by temperature changes *J Neurophysiol* 1948 *11* 311-315

TASAKI I & MIZUGUCHI K Response of single Ranvier nodes to electrical stimuli *J Neurophysiol* 1948 *11* 295-303

TASAKI I MIZUGUCHI K & TASAKI K Modification of the electric response of a single Ranvier node by narcosis refractoriness and polarization *J Neurophysiol* 1948 *11* 305 310

TOWER D B & MCEACHERN D Acetylcholine and neuronal activity in craniocerebral trauma *J Clin Invest* 1948 *27* 538

TOWLER M L Clinical value and limitations of electroencephalography *Texas J M* 1948 *44* 349-354

WARD A A Jr MCCULLOCH W S & KOPELOFF N Temporal and spatial distribution of changes during 'spontaneous seizures in monkey brain *J Neurophysiol* 1948 *11* 377-386

WARD A A Jr MCCULLOCH W S & MAGOUN H W Production of an alternating tremor at rest in monkeys *J Neurophysiol* 1948 *11* 317-330

WEIL A A Neurophysiological disturbances following electric shock therapy electroencephalographic observations *Ohio M J* 1948 *44* 1017

WEYDEN J B van der Post-traumatische amnesie en electroencephalographie *Geneesk gids* 1948, *26* 325

WHEELER E T & KOSKOFF Y D Certain aspects of personality as related to the electroencephalogram *Am Psychol* 1948 *3* 278

WHITE J C LIU C T & MIXTER W J Focal epilepsy a statistical study of its causes and the results of surgical treatment epilepsy secondary to cerebral trauma and infection *N England J M* 1948 *239* 1-10

WULFF V J The electrical response of frog eyes to prolonged illumination *J Cellul Physiol* 1948 *32* 31-43

WULFF V J & FREYBURGER S W Relation between the resting and action potential in the frog eye *Anat Rec* 1948 *101* 665

AUTHORS' INSTRUCTIONS

STYLE

Authors submitting manuscripts to the editors are reminded to kindly keep in mind the desirability of CLARITY BREVITY CONSISTENCY and ACCURACY Good scientific literary style is direct and to the point Ambiguous obscure or too highly specialized expressions or terms should be particularly avoided in a journal of this type which is attempting to cross barriers of language and diverse scientific and medical specialities New or esoteric terms should be carefully defined for the benefit of readers who may have difficulty in understanding either due to nationality or training

Reports of original research should generally be organized according to the following plan

(i) *Introduction* stating the object and scope of the investigation with a brief history of the subject

(ii) Technique or Methods and *Subjects or Materials* should be presented concisely in small print

(iii) *Results* with illustrative protocols sample records tables and curves or diagrams

(iv) Discussion giving *concise* interpretation of results and their special or general significance

(v) *Summary or/and Conclusions* preferably enumerated

(vi) *Acknowledgments* (in small print)

(vii) *Legends,* for figures enumerated

(viii) *Illustration* lettering clear and complete should be enumerated with author s name on reverse side Originals or good photographic copies may be submitted preferably not excessively reduced Illustrations should be kept to a minimum since the cost of a large number of expensive illustrations will have to be shared by the authors

COPY

The manuscript should be preceded by a separate title page giving the complete title (all caps) the names and initials of author or authors and the name and address of the institution or laboratory where the work was done On a second separate page should appear a *running title* not exceeding 40 letters in length together with the name and exact complete address to which the proofs are to be sent Other instructions to the printer may be included on this page

All manuscripts should be distinctly typed with one *original* and one *first carbon copy* sent to the editors to facilitate distribution to the referees A margin of at least 3 cm should be left all around Typing should be *triple spaced* for parts to be printed in standard type and *double spaced* for those parts to be printed in small type Use *separate pages* for all copy in small type Footnotes should be typed single space, numbered in sequence and inserted in the text immediately following the sentence of their reference

Authors are requested to try to make their copy letter perfect throughout to ease the burden of the editorial staff Authors will be charged for all corrections on the proof arising from errors or changes in the original manuscript

TABLES AND FIGURES

Numerical data presented in tabular form should be typed on a separate page for each table Consecutive tables should be numbered in roman numerals (I II etc) and referred to in the text by these numerals Figures (which includes sample records and graphic illustrations) should also appear each on a separate page and numbered consecutively in arabic numerals (1 2 etc) and referred to in the text by these numerals If original illustrations are sent it is wise to send a photographic copy as well to avoid further mailing of the originals

REFERENCES

Verification of references is entirely the responsibility of the author Every reference should be verified by the original source after it has been transcribed checking details of *spelling* (especially accents) punctuation authors names and complete initials complete title journal with correct abbreviation according to A WORLD LIST OF SCIENTIFIC PERIODICALS year volume and pages (first and last)

Citation of references in the text should be by author and year e g (Cannon 1925) or (Brink and Bronk 1935) or (Davis et al 1940) Citation by numbers will be used only for review articles containing a large number of references

Arrangement of list of references at end of text should be in alphabetical order of first author If

more than one reference for the same author they should be in chronological order Form of citation for *journals* is indicated by the following example

SHERRINGTON C S Decerebrate rigidity and reflex coordination of movements *J Physiol* 1898 *22* 319-322

for books

MAGNUS R Korperstellung Berlin J Springer 1924 740 pp

Authors names should be in capitals with all initials followed by title journal (abbreviated) underlined once year volume (arabic numerals) underlined once, initial and final pages (For list of abbreviations commonly used in neurophysiology see *J Neurophysiol* 1939 2 89 99)

ACCEPTANCE OF PAPERS

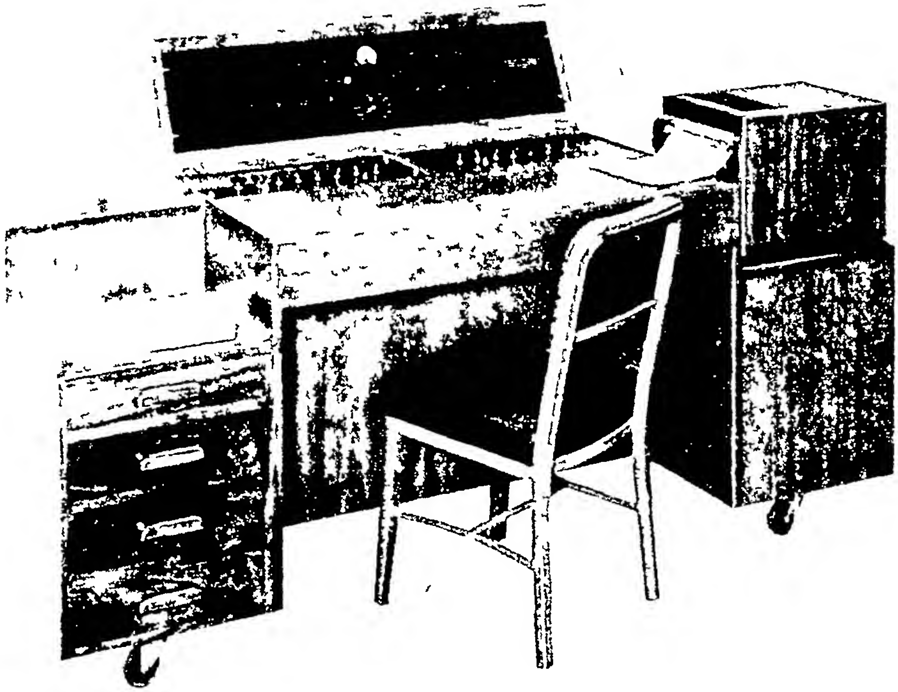
Each manuscript when submitted either to the editor or co editor is first reviewed by him and then sent to *at least two* other members of the editorial board for a critical opinion or to other referees specialized in a particular subject Their opinions are sent independently directly to the editor or co-editor In the case of suggested revision or rejection explanation of reasons will be sent the author upon return of his manuscript Manuscripts accepted by the co editor (Dr Grey Walter) and his European editorial board will be automatically accepted by the editor (Dr Herbert Jasper) and the American and Pacific editorial board each acting autonomously

COMMENTARY

Short comments or criticism of published manuscripts journal policy interesting isolated observations suggestions or reports on research developments clinical comments news of new laboratories changes in personnel requests for assistance or applications for positions etc are solicited for this section of our journal

SOCIETY PROCEEDINGS

The proceedings of various EEG *Societies throughout* the world with English translations when in another language will be published as promptly as space permits Abstracts of communications presented before *Annual meetings* of national societies, or before the *International Congress* should not exceed 250 words with an additional 100 words allowed for discussion Abstracts of major symposium papers should not exceed 500 words Abstracts of papers presented before regional society meetings and quarterly meetings of national societies should not exceed 150 words Proceedings should be carefully edited first by the respective Society Secretaries and mailed directly to Dr John Knott University of Iowa Iowa City Iowa U S A



(4) Disorganisation of the record

(5) Increased instability on hyperventilation with comparable blood sugars

With equivalent experimental conditions of dosage cholinesterase inhibition etc these changes are much less marked in the schizophrenic group Schizos given higher doses over a more prolonged period developed the EEG abnormalities

DEMONSTRATIONS

1 Duplicating EEG Recordings — D GORDON (W End Hospital)

An automatic printer for records will be shown consisting of a special printing frame for taking records without cutting or creasing and an automatic timer for exposure

The paper used is Reflex Document Paper giving a white on black trace although black on white traces can be obtained by means of an intermediate negative

2 Inexpensive Electrode Selector — J L COATES (Introduced by M E Heppenstall)

This is designed to give independent connexion of any of 14 electrodes to any amplifier grid by means of telephone jacks and plugs A selected group of electrodes is indicated on an illuminated panel and also on the record itself every 15 seconds

Total cost is less that £4

WESTERN ELECTROENCEPHALOGRAPHIC SOCIETY (USA)

Officers for 1949 are

President Dr ROBERT S DOW Portland Oregon

Vice-President Dr DAVID TALBOT Los Angeles, California

Secretary Treasurer Dr NICHOLAS BERCEL Dept of Electroencephalography Cedars of Lebanon Hospital Los Angeles 27 California

1 Studies on irradiation of differentiated cerebral excitation and inhibition as indicated by respiration — WILLIAM F ALLEN Department of Anatomy, University of Oregon Medical School, Portland, Oregon

The results of this study are based on thoracic respiratory tracings taken at the time of recording positive and negative foreleg conditioned reflexes after correct conditioned differentiation was obtained from a variety of auditory olfactory general cutaneous and optic analysers Control respiratory tracings before conditioning were as follows Sound and light showed no effect after the first few tests olfactory caused inhibition and general cutaneous demonstrated no change inhibition or excitation

After correct conditioned differentiation was established — *Excitation* of respiration ordinarily occurred during the intervals of correct positive conditioned reflex tests and during an error for a negative conditioned test The amount character and type of excitation varied with the animal and analyser but was consistent for the same test *Inhibition* of respiration usually accompanied correct negative conditioned reflex tests from all excitable and easily inhibited dogs while the neutral type revealed slight or no inhibition, but inhibition of respiration accompanied an error for a positive conditioned test A rapid succession of alternate negative and positive conditioned tests demonstrated (1) ability to respond correctly to each and (2) that respiration not only changed correctly but often made the change when in a state of inhibition or excitation A respiratory tracing recorded during a hasty error for a negative conditioned test often exhibits an early excitable phase approximating the foreleg movement which was followed too late by a long pronounced inhibitory wave Likewise correct positive conditioned reflex records may show short intervals of respiratory excitation accompanying two or more foreleg flexions

There are apparently two kinds of cortical excitation and inhibition correct and incorrect

2 Significance of Abnormal EEGs in Disorders of Behavior — MARGARET A KENNARD Department of Surgery, University of Oregon Medical School [1]

According to the data of many observers the per cent of abnormal EEGs in patients in psychiatric hospitals is relatively high and cannot as yet be explained on the basis of any known organic changes About fifty per cent of adult patients with major psychoses or neuroses have abnormal EEGs In children with disorders of behavior the incidence is 60 70% Whereas in the normal population the incidence of abnormality is generally said to be about 10% in adults and 12-15% in children

During the past three years on the psychiatric wards of Bellevue Hospital the EEGs of a series of patients between the ages of 5 and 24 have been examined The incidence of abnormal EEGs in this group agreed with the findings of earlier observers Of the 582 patients with no demonstrable organic nervous system disorders there were 65% abnormal

[1] This work was carried out while the author was attached to the Department of Psychiatry on New York University School of Medicine and on the psychiatric wards of Bellevue Hospital

records in patients below the age of 14 Above that age the incidence dropped abruptly to about 50% where it remains throughout the age levels tested Evidence appeared which indicated that sensitivity or reactivity of EEG pattern was the factor most important in producing the dysrhythmic abnormal records There were various influences affecting this sensitivity among which were (1) age of patient (2) familial or inherited tendencies (3) organic insult such as head trauma or infectious processes (4) anxiety or tension states

The total EEG pattern then is a result of all the stabilizing or distorting factors which may have been brought to bear on the cerebral activity

3 Studies in Electronarcosis Therapy Electroencephalographic Investigations — ALEXANDER SIMON, CHARLES L YEAGER and KARL M BOWMAN The Langley Porter Clinic and The Division of Psychiatry of the University of California Medical School

Approximately 50 patients receiving electronarcosis therapy were studied by means of the encephalogram An average of 20 treatments were administered to each patient at a frequency of 3 times per week The majority of the patients were schizophrenics but several cases of manic depressive psychosis and of severe psychoneurosis were included in the group

Electroencephalographic tracings were taken before treatment immediately after an individual treatment during the course of treatment and for varying periods after cessation of treatment Correlations were made with the clinical condition of the patient The electroencephalographic changes were also compared with those occuring in electro shock therapy

Immediately after the first treatment the electroencephalographic abnormality was mild and persisted no longer than 4 hours but by the end of the fifth treatment when gross abnormalities were noted they failed to diminish from treatment to treatment

It has also been noted that when clonic movements do not occur during the course of treatment the mental condition of the patient does not change However when convulsions are induced the mental state may progressively improve The electroencephalographic changes do not occur in those situations where clonic movements are absent

4 Electroencephalographic Findings in Twenty Six Cases of Verified Subdural Hematomas — A A MARINACCI and H K MARINACCI Los Angeles County Hospital, Los Angeles, Calif

Twenty-six cases of subdural hematomas are reported from Dr Carl W Rand s Neurosurgical Service of the Los Angeles County General Hospital An electroencephalogram was taken in all these cases from one to ten weeks after head injury and subsequently subdural hematomas were verified or evacuated surgically

This report is limited to a definite focus of suppressed activity over the hematomas There were twenty-one cases (80%) of unilateral and five cases (20%) of bilateral hematomas In the group of unilateral lesions the electroencephalogram showed a definite focus of suppressed activity consistant with the location of the hematomas In addition the remaining cortical activity was not definitely impaired in seventeen cases but it was greatly impaired in four cases The focal activity varied in the five cases with bilateral lesions In oné case with bilateral suppressed foci two large hematomas were evacuated In the remaining four cases there was a focus of suppressed activity over the larger hematoma while on the side of the smaller hematoma the activity varied from moderately suppressed to slow high voltage activity We wish to state that a focus of suppressed activity is not entirely pathognomonic of subdural hematoma

In our experience a focus of suppressed cerebral activity has been found in cases of subdural hematoma severe cerebral contusion large subcortical hematoma hydroma cortical atrophy and porencephalic cyst

5 The Relation of the Permeability of the Blood Brain Barrier to Cerebral Physiology as Reflected by Electroencephalography — ROBERT B AIRD

Cerebral concussion and electric shock therapy when induced experimentally in cats were associated with a marked prolonged increase in the permeability of the blood brain barrier as well as generalized cerebral dysrhythmias of non-specific types as recorded electroencephalographically Preliminary injections of trypan red which previously had been shown by Aird et al to lower the permeability of the blood brain barrier prevented these changes This suggested that the electroencephalographic changes were dependent upon the permeability of the cerebro-vascular system or upon physio chemical factors associated with the permeability of the system Aird points out that the neurogenic mechanisms responsible for the normal electrical rhythms of the brain are dependent upon a normal vascular supply and alterations of the latter may produce changes in the physio chemical status of the cortex which are reflected in the dysrhythmic activity of a non specific and usually diffuse form The evidence obtained in these studies would appear to indicate that the dysrhythmias of cerebral concussion and electric therapy are of this type In ad-

dition it is suggested that this same vascular mechanism may explain many of the non-specific dysrhythmias which have been observed electroencephalographically in various other abnormal conditions of the central nervous system

6 The Relationship Between the Bulbar-Reticular Suppressor Region and the EEG — ARTHUR A WARD JR

The pathway from the cortical suppressor areas to the caudate nucleus (over which suppression of electrical activity of the cortex is mediated) is said to be a collateral of the projection to the medial reticular formation of the brain stem Electrical stimulation of the medial reticular formation in anesthetized cats has no effect on the cortical EEG However in the cat paralyzed with beta-erythroidine such brain stem stimulation is followed by a prolonged generalized increase in both the voltage and frequency of the EEG from the entire cortex This striking increase lasts for 40 seconds or longer and is followed by a gradual return to a normal EEG This change has none of the characteristics of after-discharge or of stimulation of afferent tracts The possible relation of this phenomenon to the epileptic activitation obtained during sleep is discussed It is pointed out that the bulbar reticular formation in a sense represents a caudal extension of the midline diffuse circuits which are present in the diencephalon It has already been shown that stimulation at the latter level results in widespread diffuse changes in the cortical EEG which may occasionally resemble petit mal

7 Observations in Electromyography — B FEINSTEIN, E M WEBB, V T INMAN and H J RALSTON

The phasic action of the muscle groups in the lower limb has been studied during various walking activities by means of electromyography

Skin electrodes were placed over the muscles and the action potentials were amplified by means of resistance-capacitance coupled amplifiers Recordings were made with a twelve channel Heiland Oscillograph The complex electromyograph action potentials were simplified by a rectifier-filter device

Eight major muscle groups acting on the lower extremity and pelvis were investigated in ten normal male subjetcs The results were sufficiently constant so that definite patterns of activity could be assigned to the various muscle groups during the different activities

The individual muscles of the lower limb were then examined and their exact phase of action recorded Two wire electrodes were inserted into the belly of the muscle Thus only the activity of that particular muscle was recorded Thin copper wire electrodes insulated to the tip were used These were first threaded through a hypodermic needle and the tip of the wire was hooked over the bevel edge The needle was then inserted into the muscle and the position determined by stimulation The needle was then withdrawn and the hooked wire electrodes remained in place The precise phase of the stride was correlated with the electrical activity of the muscle This was achieved by moving pictures of the various activities synchronized with the electromyographic recordings

There is no relationship between the voltage output of a muscle and its isometric tension except for a given length of muscle These observations were made while studying the length-tension relationships of human voluntary muscle in subjects that had cineplastic muscle tunnels

The electromyographic records of 53 muscles which had been completely dennervated 2 to 3-½ years previously were compared with the power developed by the muscle using an electric strain gauge dynamometer The patients were veterans who had had nerve sutures The results showed a rough general correlation between power and electromyograms, but there was sufficient variation so that no useful correlation could be made in individual patients It was shown that valid conclusions as to probable power could not be made from the electromyogram

DANISH EEG SOCIETY

Neurophysiological Institute, Copenhagen, September 30, 1948

TITLES OF COMMUNICATIONS

On the correlation between clinical and electro encephalographic observations in patients treated with electroshock — Poul HONCKE

The EEG of epileptics under CO_2 breathing — Stubbe TEGLBJERG

An account of a journey to England and a visit to the various EEG centers — Hertel WULFF

An account of a journey to the United States and a visit to the various EEG centers

Discussion of the training of EEG personnel

SOCIÉTÉ D'EEG ET DES SCIENCES CONNEXES DE LANGUE FRANÇAISE [1]
DEUXIÈME RÉUNION ANNUELLE
Paris, 8 octobre 1948

1 L'epilepsie induite par la stimulation auditive intermittente rythmee ou epilepsie "psophogenique" — H GASTAUT, J ROGER, J CORRIOL et Y GASTAUT

Deux malades ont presenté des crises induites par la stimulation auditive intermittente (S A I) alors que 50 en ont présente a la stimulation lumineuse intermittente Le stimulus efficace etait chaque fois un son de hauteur comprise entre 1 et 5 kilocycles interrompu de 8 a 20 fois par seconde

La reponse obtenue etait tantôt a type d absence clinique avec pointe-onde paroxystique bilateral synchrone tantot a type de bouffees infra cliniques d ondes hypersynchrones predominant dans les regions temporales et rappelant de tres pres les caracteres d un K complexe surcharge de pointes

La stimulation photo acoustique synchronisee n a pas ete plus active que la stimulation photique

En conclusion 1° La S A I est beaucoup moins efficace que la S L I 2° Elle n est efficace que chez les malades presentant deja les caracteres cliniques et electriques de l epilepsie photogenique 3° De ce fait le mecanisme propose pour cette dernière semble pouvoir lui etre applique 4° Son efficacite moindre semble pouvoir etre rapportee a l importance egalement moindre des voies auditives centrales

2 Étude Électroencephalographique d'un cas d'epilepsie musicogenique — R HAMOIR et J TITECA

Il s agit d une femme de 38 ans présentant depuis l âge de 20 ans des crises de grand mal nocturnes associees a des équivalents psycho moteurs declenches par l audition d une musique L audition d un disque de gramophone permet de declencher 4 crises annoncees au bout de 6 secondes par un malaise epigastrique en meme temps que survient un blocage partiel du rythme alpha A ce moment apparait une deviation de la tete vers la droite et des mouvements stereotypés de grattage pendant que la malade perd conscience et que se developpent sur l EEG des rythmes lents a 6 5 4 et meme 3 c/s de forme a sommet crenele et de voltage superieur a 100 microvolts Duree de la crise une minute puis recuperation progressive de la conscience et du rythme alpha

Les bruits non musicaux des sifflements ne provoquent pas de crises La repétition d une musique qui

[1] Secrétaire Dr Henri Gastaut 149 Promenade de la Corniche Marseille France

1 Epilepsy Induced by Rhythmic, Intermittent, Auditory Stimulation or Epilepsy "Psophogenique" — H GASTAUT, J ROGER, J CORRIOL and Y GASTAUT

Two patients had attacks induced by intermittent auditory stimulation while there were fifty patients who had attacks with intermittent light stimulation The effective stimulus was in each case a sound with a frequency between one and five kilocycles interrupted eight to twenty times per second

The response obtained was sometimes a form of clinical petit mal or absence with paroxysmal bilaterally synchronous wave and spike discharge or a type of subclinical burst of hypersynchronous waves, most prominent from the temporal region and suggesting very closely the characteristics of a K complex with many spikes A combination of photic and acoustic stimuli synchronized was not more active than photic stimulation alone In conclusion

1 Rhythmic auditory stimulation is much less effective than rhythmic light stimulation 2 It is effective only in patients presenting already clinical characteristics and electrical characteristics of photogenic epilepsy 3 Because of this fact the mechanism proposed for the latter seems to be applied to the former 4 Its lesser effectiveness seems related to the lesser importance of central auditory pathways

2 Electroencephalographic Study of a Case of Musicogenique Epilepsy — R HAMOIR and J TITECA

The patient a woman of 38 years from the age of 20 had attacks of nocturnal grand mal epilepsy associated with psychomotor equivalents which were induced by hearing music Listening to a phonograph record set off four attacks preceded by about six seconds with an epigastric discomfort at the same time as a partial blocking of the alpha rhythm At this time there occurred a turning of the head to the right and stereotyped movements during which the patient lost consciousness and there appeared in the EEG slow rhythms at 6 5 4 and even 3 per second with a notched wave form and a voltage above 100 microvolts The attack lasted one minute followed by progressive recovery of consciousness and the alpha rhythm

Non musical noises such as whistles did not provoke an attack Repetition of a piece of music

s est averee une premiere fois epileptogene n est plus efficace immediatement apres une crise Il faut a ce moment patienter environ une demi-heure avant de reussir a en declencher une nouvelle

3 Action de l'insuline intra veineuse sur l'EEG de quelques traumatises anciens du crane — A Baisset, L Bugnard, Ch et F A Grezes Rueff et J Planques

Application de l epreuve de l hypoglycemie provoquee par insuline intra-veineuse (une unite par 3 kg de poids) a 16 traumatises anciens du crâne porteurs de sequelles diverses en particulier d un syndrome subjectif

L EEG de tous ces sujets etait normal meme apres hyperpnee Chez 7 d entre eux l insuline intra-veineuse a fait apparaitre sur le trace des anomalies diverses

4 Detection bio electrique d'une tumeur cerebrale sous corticale par l'EEG active (cardiazol) et l'ECG — J Paillas, H Gastaut et J Duplay

Sujet adulte mâle presentant des crises jaksoniennes gauches sans signes d hypertension intra-crânienne

EEG standard normal EEG active par l injection intra-veineuse de 2 cc de cardiazol mettant en evidence un foyer particulierement net d ondes delta polyrythmiques obtenues en opposition de phase sur une etendue tres limitee de la region parieto occipitale droite

La ventriculographie montre des anomalies difficilement interpretables du ventricule droit

La crâniotomie dirigee sur le foyer electrique decouvre un cortex parfaitement normal sur lequel l ECG permet de retrouver en l absence de toute activation un foyer d anomalies de siege et de forme correspondant a celui decele pendant l EEG active La ponction au-dessous du foyer rencontre une tumeur sous-corticale arrivant jusqu a 3 cm du cortex Exerese neuro-chirurgicale

L activation au cardiazol ne vaut donc pas que pour les lesions epileptogenes corticales mais aussi pour les foyers tumoraux même sous-corticaux

5 Note preliminaire sur les resultats fournis par l'electrographie directe des lobes occipitaux de l'homme pendant la stimulation lumineuse intermittente — H Gastaut et J Duplay

Exploration a l aide d aiguilles-electrodes bipolaires introduite par des trous de ventriculographie de l activite des lobes occipitaux depuis le cortex jusqu aux ventricules La comparaison des flickers ainsi obtenus avec ceux recueillis sur le scalp montre

which had induced a seizure the first time is no longer effective immediately following a seizure It is necessary to wait about one-half hour after an attack before a new one can be provoked

3 The Action of Intravenous Insulin on the EEG of Patients with Old Head Injuries — A Baisset, L Bugnard, Ch and F A Grezes Rueff and J Planques

Results are presented from the application of the hypoglycemic test induced by intravenous insulin (one unit per 3 kilograms body weight) to 16 patients with old head injuries and with various symptoms in particular those of a subjective character The EEG in all these subjects was normal but after hyperventilation in seven of them with intravenous insulin there appeared diverse abnormalities in the records

4 The Bio Electric Detection of a Subcortical Tumor by Means of the EEG Activated by Cardiazol and the ECG — J Paillas, H Gastaut and J Duplay

The subject was an adult male presenting Jacksonian attacks of the left side without signs of intracranial hypertension The usual EEG was normal Following the injection of 2cc of cardiazol there appeared in the EEG a focus particularly clear with polyrhythmic delta waves showing a phase reversal localization over a very limited region of the right parieto-occipital area The ventriculogram showed some anomalies of the right ventricle which were difficult to interpret

The craniotomy directed towards the electrographic focus revealed the cortex to be perfectly normal but an electrocorticogram made it possible to find again the focus corresponding to that obtained pre-operatively by the activated EEG Puncture beneath this focus lead to a subcortical tumor which reached just three centimeters below the cortex It was removed

Activation by cardiazol is not only effective for cortical epileptogenic lesions but also for focal neoplastic lesions even those beneath the cortex

5 A Preliminary Note on the Results Obtained by Direct Electrographic Recording from the Occipital Lobe in Man During Intermittent Light Stimulation — H Gastaut and J Duplay

Bipolar recording electrodes were introduced through ventriculograph burr holes and the activity of the occipital lobes was recorded Comparison of the flicker responses thus obtained with those obtained on the scalp showed considerable advantage to this

les avantages considerables de cette nouvelle methode appreciation de la forme de l amplitude et de la phase de la reponse a differentes profondeurs sans l interference de l activite de toute une population neuronique qui realise des phenomenes de masquage

Presentation de nombreux exemples des resultats obtenus permettant des constatations surprenantes sur la signification generale du processus

new method appreciation of the form the amplitude and the phase of the response at different depths in the cortex without interference from activity derived from an entire population of neurones which causes phenomena of masking Presentation of numerous examples of results obtained make possible surprising conclusions regarding the general significance of this process

6 Correlation entre le taux glycemique et le trace EEG — LUQUET et Y PARRAT

Distinction de trois categories de cas

1 — *Hypoglycemie spontanee absolue ou relative*

a) *hypoglycemie spontanee pure par adenome du pancreas hyperinsulinemie ou hyperadrenalinemie* La symptomatologie est variable l hypoglycemie a jeun franche le trace normal des que la glycemie est rendue normale par ingestion de sucre les anomalies a l hyperpnee disparues dès que la glycémie est superieure a 1 gr 20

b) *Epilepsie hypoglycemique* La glycemie a jeun est abaissee le trace partiellement normalise lorsque la glycemie est rendue normale les anomalies a l hyperpnee persistent souvent lorsque la glycemie est superieure a 1 gr 40

c) *Epilepsie avec hypoglycemie relative* La glycemie a jeun est normale le trace ameliore lorsqu une hyperglycemie est provoquee par ingestion de sucre Ces malades doivent donc etre traites en plus des anti-convulsivants habituels par l absorption de sucre même lorsque leur glycemie est normale

2 — Hypoglycemie provoquee (cure de Sackel)

3 — Hyperglycemie provoquee

Diabetiques épileptiques ou non soumis au traitement insulinique Tout se passe comme si le diabete et l epilepsie etaient des maladies antagonistes le 1er corrigeant en partie les manifestations de la seconde

6 Correlation Between Blood Sugar Level and the EEG Record — LUQUET and Y PARRAT

Distinction is made between three categories of patients

1 *Spontaneous hypoglycemia absolute or relative*

(a) *Pure spontaneous hypoglycemia due to adenoma of the pancreas hyper-insulinemia or hyper-adrenalinemia* The symptomatology is variable When hypoglycemia is due solely to the fasting state the EEG becomes normal as soon as glycemia is rendered normal after ingestion of glucose Then the abnormalities recorded during hyperventilation disappear as soon as the glycemic state is over 120 mg per cent

(b) *Hypoglycemic epilepsy* Normally glycemia is lowered when fasting and the EEG becomes partially normal when glycemia is rendered normal Abnormalities seen during hyperventilation often persist when glycemia is over 140 mg per cent

(c) *Epilepsy with relative hypoglycemia* When glycemia is normal when fasting the EEG is improved with ingestion of glucose to induce hyperglycemia These patients should then be treated with glucose ingestion besides the usual anti-convulsive drugs even if their glycemia is normal

2 *Induced hypoglycemia* (Sackel therapy)

3 *Induced hyperglycemia*

Diabetic patients whether epileptic or not under insulin treatment One may consider diabetes mellitus and epilepsy to be antagonistic diseases the former disease partially improving the clinical manifestations of the latter

7 Activation de l'EEG par le pentothal — G HEUYERE, A REMOND et R DELARUE

L injection intra veineuse d une petite dose de pentothal entraine sur les traces deux types de reactions I) reaction rapide constituee par un rythme rapide ample et regulier predominant sur la moitie anterieure de l encephale II) reaction lente constituee par un rythme lent et ample ou de grandes ondes lentes isolées

Chacune de ces deux modifications peuvent etre isolées mais elles sont plus souvent intriquees donnant éventuellement au trace l apparence plus ou moins suggestive d une serie de pointe ondes Dans

7 Activation of the EEG by Pentothal — G HEUYERE, A REMOND and R DELARUE

The intravenous injection of a small dose of pentothal produces two different types of reactions on the record 1 A rapid reaction composed of a fast large and regular rhythm predominating from the anterior half of the cerebrum 2 A slow reaction made up of a slow and large rhythm or of large and slow isolated waves

Each of these alterations may be isolated but most often they are integrated eventually giving the tracing the appearance more or less suggestive of a series of spikes and wave forms In certain cases

certains cas ce dernier aspect est suffisamment caractenstique pour permettre d affirmer l existence d un mecanisme electrique de type epileptique

8 Rythmes EEG et lesions anatomiques dans 20 cas de tumeurs temporales — O R Carvalho

Anatomiquement il s agissait de 7 glioblastomes *multiples une metastase d epithelioma 4 astrocytomes* 6 meningiomes un cholesteatome et un hematome intra-cerebral

Electriquement on trouvait 3 types d alterations I) Silence electrique avec oscillations lentes et irregulieres de la ligne de base et suppression de l alpha II) Ondes lentes polyrythmiques et irregulieres III) Activite lente monorythmique et harmonique De tous ces signes c est le silence electrique qui s est revele être le facteur de localisation le plus fidele et le plus direct tandis que les anomalies lentes et irregulieres ne constituent que des signes de voisinage et l activite lente un signe transmis a distance

9 Valeur pronostique de l'EEG dans les tumeurs de la fosse posterieure — M Bohm

Les traces peu alterés ou normaux accompagnent d habitude les tumeurs benignes a evolution lente, l issue opératoire est favorable dans 64% des cas Les traces moderement alteres accompagnent des tumeurs presque toujours malignes et a evolution rapide l issue favorable n est plus rencontree que dans 27% des cas Les traces tres perturbes s accompagnent de mortalite dans 100% des cas

Les rythmes lents generalises de 4 a 7 sont visibles dans les tumeurs du tronc cerebral tandis que les tumeurs des hemispheres cerebelleux alterent surtout le rythme des regions frontales

10 Épreuve de l'hyperpnee et derivation basale — J Faure, H Jasper et L Henderson

Le trace basal obtenu par l electrode nasale reagit a l hyperpnee comme le trace cortical Une derivation speciale reliant l electrode auriculaire a l electrode temporale et celle-ci a l electrode basale, permet de bien mettre en valeur l effet de l hyperpnee sur la base du cerveau En outre cette derivation a l avantage I) d etablir une comparaison entre les potentiels captes par l electrode auriculaire et ceux captes par l electrode basale II) d enregistrer les foyers situes dans les parties profondes du lobe temporal pres de la ligne mediane

11 Contribution a l'EEG de l'anxiete — J Faure

Presentation de traces où chez les anxieux le

this latter appearance is sufficiently characteristic to show an electrical mechanism of an epileptic type

8 EEG Rhythms and Anatomical Lesions in 20 cases of Temporal Lobe Tumor — O R Carvalho

There were 7 glioblastomas multiforme one *metastic epithelioma 4 astrocytomas 6 meningiomas* 1 cholesteatoma and one intracerebral hematoma

Electrically three types of alterations were found 1 *Electrical silence* with slow and irregular oscillations of the base line and suppression of the alpha *rhythm* 2 *Slow polyrhythmic* and irregular waves 3 *Slow activity* monorhythmic and harmonic Of all these signs electrical silence was the most trustworthy and the most direct while the slow and irregular anomalies constituted signs of adjacent areas and slow rhythmic activity was a sign transmitted at a distance

9 Prognostic Value of the EEG in Tumors of the Posterior Fossa — M Bohm

Normal or slightly changed tracings are usually seen with non-malignant tumors of slow growth Operation is successful in 64 % of cases Moderately altered tracings are encountered nearly always with malignant tumors of rapid growth, operation is successful in but 27% of cases There was 100% mortality in patients with severely abnormal records

Slow generalized rhythms of 4 to 7 per second are found in tumors of the brain stem while tumors of the cerebral hemispheres alter mostly the rhythm of the frontal regions

10 Hyperpnea and the Basal Derivation — J Faure, H Jasper and L Henderson

The basal tracing derived from the nasal electrode reacts to hyperpnea just as the cortical tracing does A special derivation joining the auricular electrode to the temporal electrode and the latter to the basal electrode shows markedly well the effect of hyperpnea on the base of the cerebrum Besides this derivation has the following advantages 1 Comparison possible between the potentials at the auricular electrode and those at the basal electrode 2 Registration of foci deeply seated in the temporal lobe near the median line

11 Contribution to the EEG in Anxiety — J Faure

Presentation of tracings of anxiety patients in

rythme alpha est remplacé d une part par un rythme theta et d autre part par un rythme beta

which the alpha rhythm is replaced on one hand by a theta rhythm and on the other hand by a beta rhythm

12 Les formes EMG de la tetanie — R TURPIN, J LEFEBVRE, J LÉRIQUE et P DORLAND

A cote de la forme tonique caracterise par le doublet les auteurs insistent sur la forme fibrillaire decrite par KUFFLER

12 Forms of EMG in Tetany — R TURPIN, J LEFEBVRE, J LÉRIQUE and P DORLAND

Besides the tonic form characterized by the doublet the authors have emphasized the fibrillary form described by Kuffler

13 Oscillographie de l epilepsie corticale faradique et strychnique chez le chat — GUY NOËL

L excitation faradique de l ecorce du chat a encephale isole entraine des modifications variables suivant l intensite du stimulus pour de faibles intensites simple intensification de l activite normale pour une intensite plus grande depression marquee pour des intensites elevees after discharge synchrone et généralisee caracterisant la crise epileptique

La duree des crises est egalement fonction de l intensite mais aussi de la frequence et de la durée du stimulus

La perturbation epileptique une fois déclenchee tend a se propager et a envahir les regions voisines

Deux foyers faradique et strychnique reagissent réciproquement l un sur l autre

13 Oscillography of Cortical Epilepsy Following Faradic Stimulation and Strychnine in the cat — GUY NOËL

The faradic stimulation of the cortex of a cat with an isolated encephalon causes modifications varying with the intensity of the stimulus with weak intensities simple intensification of normal activity with stronger intensities marked depression with still stronger intensities synchronous and generalized after-discharge characteristic of an epileptic seizure

The duration of the seizures is proportional not only to the intensity but also to the frequency and the duration of the stimulus Once started the epileptic perturbation tends to invade the adjoining regions Two foci faradic and strychninized tend to react reciprocally one upon the other

14 Effet du curare sur la transmission synaptique de la moelle epiniere chez le chien spinal — A BAISSET, YVES LAPORTE et F GREZES RUEFF

La d-tubocurarine n a pas d action sur la transmission synaptique de la moelle epiniere chez le chien spinal

La d tubocurarine ne retentit sur la transmission medullaire qu a travers le collapsus vasculaire qu elle est susceptible de provoquer lors de son injection intra veineuse rapide

14 Effects of Curare or Synaptic Transmission of the Spinal Cord in a Spinal Dog — A BAISSET, YVES LAPORTE and F GREZES RUEFF

Subocuraine has no effect on the synaptic transmission of the spinal cord in the spinal dog

It may act on spinal transmission only through a vascular collapse which may be caused by its rapid intravenous injection

15 ECG de l'epilepsie provoquee par electro choc chez le rat curarise non anesthesie — H GASTAUT, J CORRIOL, J CAIN et J MERCIER

Presentation d une abondante iconographie concernant 62 crises entierement enregistrées sans interference de myogramme ni de mecanogramme du fait de la curarisation des animaux Signification particuliere des documents enregistres chez l animal non anesthesie a metabolisme cortical non modifie

59 traces sur 62 sont pratiquement superposables et repondent a une crise type qui est analysee

15 ECG of Epilepsy Induced by Electroshock in a Curarized but not Anaesthetized Rat — H GASTAUT, J CORRIOL, J CAIN and J MERCIER

Presentation of an abundant iconography of 62 seizures completely recorded without interference of myogram or mechanogram due to curarization of the animals

Of particular significance were the records from unaesthetized animals with cortical metabolism unmodified

59 tracings out of 62 are practically superposable corresponding to a typical seizure which is analyzed

16 Le probleme des analyseurs de frequence en EEG — G MINOT

Multiplicateur de frequences de coefficient 40 base sur un procede original photoelectrique Ceci permet l analyse a l aide des moyens classiques d enregis

16 The Problem of Frequency Analyzers in EEG — G MINOT

A multiplier of frequencies with a coefficient 40 based on an original photoelectrical process is described This permits the analysis with the aid of

trement du spectre des frequences ainsi qu a l aide de casques et de haut-parleur realisant une veritable auscultation cérebrale

the classical means of registration of the spectrum of frequencies and also with the aid of helmets and of a loudspeaker making possible a veritable cerebral auscultation

CENTRAL ASSOCIATION OF ELECTROENCEPHALOGRAPHERS

Chicago, November 27 28, 1948

TITLES OF COMMUNICATIONS

The Basis of Analysis of the Electroencephalogram — F F OFFNER, Offner Electronics, Inc , Chi cago, Ill

Pathways of Electrical Current in the Brain — F M LORIMER, M M SIEGEL and S N STEIN, University of Ill Med School

Subcortical Centers as Pacemakers of Cortical Ac tivity — E GELLHORN, University of Minnesota Medical School

"Feedback" Effects Related to Autonomic Changes — C W DARROW, Institute for Juvenile Re search, Chicago, Ill

Electroencephalogram During a Cycle of Addiction to Keto Bemidone Hydrochloride — S ALTSHUL and A WIKLER, U S Public Health Service Hos pital, Lexington, Ky

A Preliminary Report on the Somatic Afferent and Auditory Areas of the Cerebral Cortex of the Marmoset — Clinton WOOLSEY, Department of Physiology, Service Memorial Institutes, Uni versity of Wisconsin

Arousal Response During Sleep as a Test of Sen sory Function — R E MARCUS, E L GIBBS, and F A GIBBS, University of Illinois Medical School

The Electroencephalogram in Chronic Alcoholism — W H FUNDERBURK, Traverse City State Hos pital, Traverse City, Michigan

Electroencephalographic and Metabolic Studies Be fore and After Frontal Lobotomy — R ROSSEN, N BRADLEY, R SCHROEDER, and A REICHENBERG, Hastings State Hospital, Hastings, Minnesota

EEG Findings in Hypertension and Their Correla tion with the Clinical Status, Operative Risk and Post operative Confusion — B K BAGCHI, K A KOOI, and S W HOOBLER, The Neuropsy chiatric Institute, University of Michigan

Findings in Thirty Five Head Injuries with Sur gically Verified Brain Damage — Dr E C CLARK, Henry Ford Hospital, Detroit

A Preliminary Report on Therapeutic Results of Temporal Lobotomy for Psychomotor Epilepsy — Percival BAILEY and F A GIBBS

ABSTRACT

Electroencephalographic and Clinical Responses to Light Stimulation in Normal Subjects — R G BICKFORD

The electro encephalographic and clinical responses to light stimulation produced by a strobolux dis charge tube and by sectored light have been in- vestigated in 50 normal subjects Their ages ranged from four to twenty-seven years The resting electro- encephalographic records of 14 per cent were classi- fied as abnormal

The electrical responses to light stimulation may be divided into three categories (1) direct driving response which appears at the flash frequency or a multiple or submultiple of it and is usually confined to the occipital and parietal areas (2) slow com plex delta discharges confined to the occipital and parietal areas but unrelated to the flash frequency, and (3) generalized paroxysmal discharges usually synchronous over the whole cortex and not directly related to flash frequency Light stimulation induced one or more of the above responses in 92 per cent of the group and had not appreciable effect on the cortical potentials in the remaining 8 per cent The driving response (type 1) was present in 92 per cent of subjects, the amplitude being greater in the older age groups It was associated with sub jective sensations of light and color which were not often unpleasant

The delta discharges (type 2) were present in 10 per cent of the subjects They were usually asso- ciated with unpleasant feelings of dizziness and dis orientation and in 1 case their appearance preceded a clinical seizure

Paroxysmal discharges (type 3) were present in 14 per cent of the subjects Clinical seizures were induced in 2 subjects showing this type of discharge In the remaining 5 subjects of this group a variety of unpleasant subjective effects were noted

The strobolux light was slightly more effective in producing the driving response (type 1) than was the sectored light Discharges of types 2 and 3 were more frequently produced by the sectored light Clinical seizures were produced only by sectored light

ANNOUNCEMENTS

DEUXIÈME CONGRÈS INTERNATIONAL D'ÉLECTROENCEPHALOGRAPHIE

Paris 1, 2, 3 septembre 1949

Comite d'organisation du Congres

President du Congrès A Baudouin (France)
Vice-President F Bremer (Belgique)
Membres du Comite
Amerique Latine J Odoriz
Canada H Jasper
Chine
Danemark H Herz
États-Unis F A Gibbs et R Schwab
Grande-Bretagne W Grey Walter et D Hill
Hollande J ten Cate
Italie M Gozzano et G Morruzi
Mexique A Rosenblueth
Roumanie A Kreindler
Suede T S Frey Jr
Suisse M Monnier
Tchecoslovaquie K Henner
Turquie F K Gokay
URSS
Secretaire general H Fishgold
Secretaire H Gastaut
Secretaire A Remond
Trésorier G Verdeaux

Date du Congres

Le Congres International d EEG se tiendra a Paris les 1er 2 et 3 septembre 1949 Un jour de la semaine suivante sera occupe par une seance commune des Congrès Internationaux de Neurologie et d Electro encephalographie

Le choix des locaux sera fait ulterieurement par le Comite d organisation

Rapports

A la suite des suggestions faites par les Comites des differentes sociétés nationales d EEG le programme des rapports a ete ainsi etabli

1° Le Jeudi 1er septembre a 9h 30 W GREY WALTER Principes et methodes de localisation
de 10 a 11h Discussion du rapport
à 14h 30 F A GIBBS Enregistrement direct chez l homme des structures corticales et sous corticales
de 15 a 16h Discussion du rapport

2° Le Vendredi 2 septembre a 9h H BRAZIER Les champs electriques cerebraux et leurs effets
de 9h 30 a 10h 30 Discussion du rapport

3° Le Samedi 3 septembre a 9h H GASTAUT et V J WALTER Effets des stimulations physiques sur l EEG
de 9h 30 a 10h 30 Discussion du rapport
a 14h 30 A REMOND Y LAPORTE et C BRISSAC Effets des stimulations chimiques sur l EEG
de 15h a 16h Discussion du rapport

4° Pour la journee commune des Congres Internationaux de Neurologie et d Electroencephalographie
F BREMER Bases physiologiques de l EEG
H JASPER EEG in neurosurgical diagnosis
F A GIBBS EEG in neurological diagnosis
F BUCHTAL Electromyography in neurological diagnosis (central nervous disease)
M HARVEY Electromyography in neurological diagnosis (peripheral nervous disease)

La discussion sera libre mais ne pourra depasser 3 minutes exception faite pour les orateurs inscrits a l avance auxquels seront accordees 5 minutes

A la suite de la discussion du rapport chaque seance sera consacree a des communications diverses

Les textes des rapports doivent etre adresses au plus tard le 1er mars au Dr FISCHGOLD Librairie MASSON & Cie 120 bd Saint Germain a Paris (6°)

Communications

Elles devront etre adressees
pour l Amerique au Dr R SCHWAB
Massachussetts General Hospital
BOSTON 14 (Mass) USA
pour l Europe au Dr REMOND
131 Boulevard Malesherbes
PARIS (17°)
qui les soumettront aux Comites de coordination etablis pour chacun des Continents

Le dernier delai auquel le titre et le resume des communications (500 mots au plus) pourront etre remis aux Secretaires susnommes des Comites de coordination est fixe au 1er mai 1949

Inscriptions

Toute personne s interessant a l Electroencephalographie peut se faire inscrire en tant que Membre titulaire en s adressant aux Secretaires des Comites de coordination dont elle depend (Dr SCHWAB pour l Amerique Dr REMOND pour l'Europe)

Les personnes s interessant au Congres peuvent être nommees membres associes

Afin de couvrir les depenses de l organisation du Congres chaque membre titulaire versera une somme de 10 dollars ou son equivalent cette cotisation donnera droit a l envoi du texte imprime des rapports discussions et communications du Congres International d Electroencephalographie

Chaque membre associe devra verser la somme de 5 dollars ou son equivalent

La liste des membres sera close le 1er mai 1949

Reception des Congressistes

Un Comite de reception siegera avant et pendant le Congres et se tiendra a la disposition des Congressistes

Pour tous renseignements complementaires s adresser au membre du Comite représentant les U S A Dr R Schwab Massachusetts General Hospital, Boston 14 (Mass) U S A

ou au Secretaire pour l Etranger de la Societe d Electroencephalographie de Langue Française Dr H Gastaut 149 Promenade de la Corniche a Marseille

SECOND INTERNATIONAL EEG CONGRESS

Paris, September 1, 2, 3, 1949

Organization Committee of the Congress

President of Congress A Baudouin (France)
Vice-President F Bremer (Belgium)
Members of the Committee
Latin America J Odoriz
Canada H Jasper
China
Denmark H Herz
United States F A Gibbs and R Schwab
Great Britain W Grey Walter and D Hill
Holland J Ten Cate
Italy M Gozzano and G Morruzi
Mexico A Rosenblueth
Roumania A Kreindler
Sweden T S Frey Jr
Switzerland M Monnier
Turkey F K Gokay
Czekoslovakia K Henner
U S S R
Secretary General H Fishgold
Secretary H Gastaut
Secretary A Remond
Treasurer G Verdeaux

Date of Congress

The committee on organization of the Second International EEG Congress is given above The dates given Sept 1-3, 1949 are on Thursday Friday, and Saturday of the week preceeding the International Neurological Congress One day of the following week will be devoted to a combined meeting of the EEG and Neurological Congress This will consist of a symposium on Electroencephalography and Electromyography

Reports

Following suggestions derived from the various national EEG Societies the following general program has been established

Thursday Sept 1 9 30 A M
Principles and methods of localization W Grey Walter
Discussion 10 to 11 A M
2 30 P M
Direct Recording from Cortical and Sub cortical Structures in Man Frederic A Gibbs
Discussion 3 to 4 P M

Friday Sept 2 9 00 A M
Electrical fields at the surface of the head their distribution in various conditions Mary A B Brazier
Afternoon session to be arranged

Saturday Sept 3 9 00 A M
Effects of physical stimuli upon the EEG H Gastaut and Vivian J Walter
Discussion, 9 30 to 10 30 A M
2 30 P M
Effects of chemical stimuli upon the EEG A Remond Y Laporte and C Brissac
Discussion, 3 to 4 P M

Combined meeting with the Neurological Congress
Physiological Bases of the EEG F Bremer
The EEG in Neurosurgical Diagnosis H Jasper
The EEG in Neurological Diagnosis F A Gibbs
Electromyography in Neurological Diagnosis (diseases of the CNS) F Buchtal
Electromyography in Neurological Diagnosis (peripheral neuromuscular diseases) M Harvey

Discussion will be open but limited to 3 minutes except for prearranged speakers who will be allowed 5 minutes

Following the discussion of each of the above principal papers individual communications will be presented

Manuscripts of the principal reports should be sent by March 1st 1949 to Dr H Fischgold Librairie Masson et Cie 120 Bd St Germain Paris (6e)

Communications

American to Dr R S SCHWAB
Massachusetts General Hospital
Boston 14 Mass U S A

European to Dr A REMOND
131 Boulevard Malesherbes
Paris (17e) FRANCE

who will submit them to coordinating committees for their respective continental areas

Abstracts, not exceeding 500 words must be received by the above secretaries not later than May 1 1949

Registration

Everyone interested in Electroencephalography may register by writing to one of the above secretaries of the Coordinating Committees

In order to cover the expenses of organizing the Congress each titular member shall pay a fee of ten dollars ($10 U S) or its equivalent this fee covering the cost of the printed proceedings of all papers communications and discussions of the International Congress of Electroencephalography Associate members (who will not receive the printed proceedings) may register with a fee of five dollars ($5 00)

Membership will be closed on May 1st 1949

Reception

A reception committee will be at the disposition of the members of the Congress before and after the Scientific Sessions

Information not provided in this announcement may be obtained from Dr R S SCHWAB Mass Gen Hospital Boston 14 Mass U S A or from Dr H GASTAUT 149 Promenade de la Corniche Marseille France

THE AMERICAN EEG SOCIETY

ANNUAL MEETING

Atlantic City, June 11 12, 1949

Communications Saturday June 11
Symposium on *Thalamo Cortical Mechanisms*
with the American League Against Epilepsy Sunday June 12

NEW SOCIETIES

SOUTHERN SOCIETY OF ELECTROENCEPHALOGRAPHY

We are pleased to announce the establishment of the Southern Society of Electroencephalography in the United States The first annual meeting was held in Dallas Texas December 5 1948 The officers are President Martin L Towler M D Galveston Vice President Richard L Masland M D Winston Salem and Secretary-Treasurer Samuel C Little M D 2111 Highland Ave Birmingham Alabama U S A

GROUPEMENT SUISSE D'ÉLECTROENCÉPHALOGRAPHIE

We are pleased to announce the foundation of a Groupement Suisse d Electroencephalographie The Swiss society has been recently organized with the following officers

President Prof Oscar WYSS Ecole de Medecine Geneva Switzerland

Secretary Dr R HESS Heliosstrasse 22 Zurich Switzerland

To the Swiss Society your colleagues throughout the world send best wishes

NOTICE

CLASSIFIED BIBLIOGRAPHY OF ELECTROENCEPHALOGRAPHY

1875 - 1948

Edited by

M A B Brazier, Ph D

A comprehensive list of all pertinent references classified under 17 subject headings

TO BE PUBLISHED SOON
AS A SUPPLEMENT TO THIS JOURNAL

Send orders to EEG JOURNAL, 3801 University St , Montreal 2, Canada

COMMENTARY

To our Japanese colleagues we extend our sincere regrets and sympathy in the loss of Professor Dr Yasuji Kakegawa of the Niigata Medical College who died on November 13 1948 As a tribute to Professor Kakegawa who has been a leader in developing electroencephalography and neurophysiological research in Japan following the war we quote the following letter from his associate Professor Masaichi Sawa who gives an interesting account of the development of electroencephalography in Japan

Dear Professor Jasper

It grieves me that this first letter to you whom I so deeply respect should be a bad report about Professor Yasuji Kakegawa my senior and excellent collaborator

Professor Kakegawa passed away on November 13th leaving behind him an outstanding achievement in electroencephalographic study of Japan To his last moment he kept his passion for his study making effort to compile the result of his research His great hope was that he may be enabled by your kindness to attend the international meeting at Paris next year As I report to you of his death I here express my deep gratitude to you for your friendship with him

Now since you refer to EEG in Japan in your letter I feel responsible of writing you though briefly about the present state of progress of EEG in Japan Probably EEG research in Japan was opened up by Professor Katsunuma in about 1936 under the instruction of Professor Kornmuller of Germany

Later on Ito Kaketa Professors Motokawa and Kakegawa continued their earnest study of it even since before the war but it did not make a progress notable enough to attract general attention the work being rather elementary Particularly during the war this research work as other scientific researches suffered from much difficulty In spite of this handicap Professors Motokawa and Kakegawa work constantly presented fine results In particular Professor Motokawa s theoretical study concerning the origin of brain wave though it has some evident defects detectable even by us is worth introducing to you brain wave scholars of both England and America for your investigation and criticism Those articles were submitted to the Tohoku Journal of Experimental Medicine So as I write you this letter I also am going to ask Professor Motokawa to send those articles to you

After the termination of the war quite a number of students of brain waves have appeared which I think is an evidence of great improvement in general interest in this line of study They have formed a special group for brain wave research in the medical section of Japan Scientific Research Council and keeping a close contact with each other they are doing earnest research However the impoverished financial state of post war Japan which has hampered every progressive effort in the country has retarded our progress also

One of the general tendencies of the post-war research is the theoretical inquiry about this Motokawa s theory of brain wave origin which is being undertaken chiefly by Professor Imabori the Institute of Applied Electricity of Hokkaido University Sapporo and Professor Sato of the Department of Physiology Niigata Medical College The other is clinical application which is being attempted in a number of medical institutions but which I am afraid is by far inferior to yours due to our technical and financial poverty The technical efficiency may be improved in the future since the cooperation by electrical engineering has become quite active but one of the important factors for our future development will be the cooperation and assistance of advanced nations in reference to the amplifying and recording apparatus

We now keenly wish to have some one of our group attend the international meeting at Paris now that Professor Kakegawa has been lost we hope some one will take his place in this privilege for the attendance will mean so much to us in getting the information and knowledge as to how other countries have been working on their EEG problems during and after the war and at the same time it will give us a good opportunity to show them what we entirely cut off from the other part of the world have been doing

With many thanks for you

Most sincerely yours

(signed) Masaichi Sawa M D
Professor of Special Course of Medicine
Department of Neurology and Psychiatry
Niigata Medical College Niigata Japan

Reprints enclosed

Kakegawa Y Electroencephalographic Study of Narcosis and Sleep *Acta Medica Hokkaidonensia* 1944 22 56 74

Kakegawa Y Electroencephalographical Changes during Mental Efforts *Folia Psychiat et Neurol Japonica* 1947 2 109 123

Kakegawa Y A new Method for continuous Oscillographic Recording of Cerebral Blood Flow *Folia Psychiat et Neurol Japonica* 1947 2 156 164

Kakegawa Y Sawa M and Horiuchi K Cerebral Blood Flow and Electrical Corticogram preceding and during Cardiazol Convulsion in Man and Cat *Folia Psychiat et Neurol Japonica* 1947 2 249 260

Sawa M Spontaneous electrical Activities obtained from Human Spinal Cord *Folia Psychiat et Neurol Japonica* 1947 2 156 179

Sawa M Functional Interrelation of Cerebral Hemispheres Mediated by Corpus Callosum in Cat *Folia Psychiat et Neurol Japonica* 1947 2 221-248

Kambara H and Sawa M A case of Identical Twins with Little s Disease *Folia Psychiat et Neurol Japonica* 1947 2 369 378

INDEX TO LITERATURE

Edited by CHARLES HENRY

ADRIAN E D Cerebral function *Brit M J* 1948 *2* 349

AITA J A & REITAN R M Psychotic reactions in the late recovery period following brain injury *Am J Psychiat* 1948 *105* 161-169

APTER N S HALSTEAD W C EISELE C W & McCULLOUGH N B Impaired cerebral functions in chronic brucellosis *Am J Psychiat* 1948 *105* 361-366

BARKER W Studies in epilepsy Personality pattern situational stress and the symptoms of narcolepsy *Psychosomat M* 1948 *10* 193-202

BARNES T C Electroencephalography *Brit M J* 1948 *2* 349

BARNES T C Phase-boundary model of a cellular surface receptor *Anat Rec* 1948 *101* 741

BARNES T C & AMOROSO M D *A revised method* of estimating the somatic factors affecting the electro encephalogram in deep breathing *Anat Rec* 1948 *101* 740

BARNES T C & AMOROSO M D A revised method sedation, a major aid to electroencephalography of infants originated at Hahnemann Medical College *Anat Rec* 1948 *101* 667

BARNES T C & AMOROSO M D A revised method waves along an oil-saline interface and their significance for electroencephalography *Anat Rec* 1948 *101* 666

BARNES T C BEUTNER R & BEUTNER K R The effect of alcohol on the acetylcholine metabolism of the brain *Anat Rec* 1948 *101* 739

BARTHOLOMAEUS H A, NOELL W K & PRAST J W Modifications in technique of placement of needle electrodes in brain studies *School of Aviation Medicine* Randolph Field Texas 1948 Project # 21-02-047 Report # 1

BAUWENS P Electromyography *Brit J Phys M* 1948 *11* 130-136

BERG E A & GRANT D A The performance of topectomized patients on the University of Wisconsin Card Sorting Test *Am Psychol* 1948 *3* 360

BERITOFF J On the role of the spontaneous activity of the central nervous system in the behavior of man and animals *Arch neerl Physiol* 1948 *28* 521-526

BEUTNER R & BARNES T C Transient phase-boundary potentials which form propagated electrical waves *Anat Rec* 1948 *101* 665

BLUM R A The effect of bilateral removal of the prefrontal granular cortex on delayed response performance and emotionality in chimpanzee *Am Psychol* 1948 *3* 237-238

BLUM R A BLUM J S & CHOW K L The production of unilateral epileptiform convulsions from otherwise quiescent foci by the administration of benzedrine *Science* 1948 *108* 560-561

BONHOEFFER K F Activation of passive iron as a model for the excitation of nerve *J Gen Physiol*, 1948 32 69-91

BOWMAN R L Adaptation of selsyn transmitters for obtaining isometric myographs on the cathode ray oscilloscope *Science* 1948 *108* 310

BREMER F Aspect theorique de l electroencephalographie *Arch neerl physiol* 1948 *28* 481-487

BROCK S Dynamic mechanisms underlying some forms of cerebral dysfunction *Am J Psychiat* 1948 *105* 246 253

BROOKHART J M & MORRIS R E Antidromic potential recordings from the bulbar pyramid of the cat *J Neurophysiol* 1948 *11* 387-398

BROOKS C McC & ECCLES J C An analysis of synaptic excitatory action *J Neurophysiol* 1948 *11* 365 376

BROOKS C McC & ECCLES J C Inhibition of antidromic responses of motoneurones *J Neurophysiol* *1948 11 431-444*

BROOKS C McC & ECCLES J C Inhibitory action on a motor nucleus and focal potentials generated therein *J Neurophysiol* 1948 *11* 401-416

BROOKS C McC ECCLES J C & MALCOLM J L Synaptic potentials of inhibited motoneurones *J Neurophysiol* 1948 *11* 417-430

BUCHTHAL F & ENGBAEK L *On the neuro muscular* transmission in normal and myasthenic subjects *Acta psychiat neur Kbh* 1948 *23* 3-11

BULLOCK T H Properties of a single synapse in the stellate ganglion of squid *J Neurophysiol*, 1948 *11* 343-364

CHAPMAN W P LIVINGSTON R B & LIVINGSTON K E The effect on respiration and blood pressure of electrical stimulation of the orbital surface of the frontal lobe and of frontal lobotomy in man *J Clin Invest* 1948 *27* 529

CORNIL L CREMIEUX A & GASTAUT H Importance semiologique de l electroencephalographie dans le diagnostic des crises epileptiques de l enfant *Sem hop Par* 1948 *24* 1609-1613

CRESS C H & GIBBS E L Electroencephalographic asymmetry during sleep *Dis Nerv Syst*, 1948 *9* 327-329

DAX E C, FREUDENBERG R K (et al) Prefrontal leucotomy a review *Postgrad M J* Lond, 1948 *24* 415 426

DAX E C & RADLEY-SMITH E J The operation of prefrontal leucotomy *Brit J Surg* 1948 *36* 74-78

DESROCHERS J L Syndrome de Wernicke ou polioencephalite hemorragique aigue supérieure presentation d un cas a evolution typique se transformant apres traitement en epilepsie psychomotrice *Union med* Canada 1948 *77* 1071-1075

Elektroenkephalograph (Der) ein elektronisches Messgerat fur Gehirnerkrankungen *Schweiz Bl Krankenpfl* 1948 *41* 190

GIBBS F A & HAYNE R The localizing value of electrical sign in electroencephalography *Dis Nerv Syst* 1948 9 289

GIRDEN E The electroencephalogram in the curarized mammal *Am Psychol* 1948 *3* 369

GOODWIN C W & STEIN S N A brain-wave correlator *Science* 1948 *108* 507

GORDON G & HOLBOURN A H S The sounds from single motor units in a contracting muscle *J Physiol* 1948 *107* 456 464

GOTTA H & ODORIZ J B The electroencephalogram in hypoparathyroidism with tetany and epilepsy *J Clin Endocr* 1948 *8* 674-686

GOULD L N Verbal hallucinations and activity of vocal musculature an electromyographic study *Am J Psychiat* 1948 *105* 367-372

GRAM L A case of concurrent vomiting in a child with electrical cerebral dysrythmia *Acta paediat* Upps 1948 *35* 250 259

GREEN J R Electroencephalography its place in neurodiagnosis *Arizona M* 1948 *5* 38 42

FISCHER J W Severe paroxysmal cardiac pain as a prodrome in idiopathic epilepsy *Am J M Sc* 1948 *216* 78 83

FOLKOW B & UVNÄS B The chemical transmission of vasoconstrictor impulses to the hind limbs and the splanchnic region of the cat *Acta physiol scand* *105* 28-39

FRANK L K HUTCHINSON G E LIVINGSTON W K McCULLOCH W S & WIENER N Teleological mechanisms *Ann N Y Acad Sci* 1948 *50* 187 278

FULLER J L & GORDON T M Jr The radio inductograph a device for recording physiological activity in unrestrained animals *Science* 1948 *108* 287

FUSTER B GIBBS E L & GIBBS F A Pentothal sleep as an aid to the diagnosis and localization of seizure discharges of the psychomotor type *Dis Nerv Syst* 1948 *9* 199-202

GALLI O Un electroencefalografo per uso clinico *Arch psicol neur* Milano 1948 *9* 288-296

GELLHORN E & BALLIN H M Age and susceptibility to convulsions *Proc Soc Exp Biol* N Y 1948 *68* 540 543

GENGERELLI J A The stimulation of nerves by means of radiant energy *Am Psychol* 1948 *3* 340

GUTMANN E Effect of delay innervation on recovery of muscle after nerve lesions *J Neurophysiol* 1948 *11* 279 294

HALLENBECK G A WOOD E H & CLAGETT O T Apparatus for recording physiologic variables during operations on man with observations on changes of blood pressure during resection for coarctation of the aorta *Surg Clin N America* 1948 *28* 851 859

HARRIS G W Stimulation of the supraopticohypophysial tract in the conscious rabbit with currents of different wave form *J Physiol* 1948 *107* 412-417

HARRIS G W Electrical stimulation of the hypothalamus and the mechanism of neural control of the adenohypophysis *J Physiol* 1948 *107* 418 429

HEATH R G & POOL J L Treatment of psychoses with bilateral ablation of a focal area of the frontal cortex *Psychosomat M* 1948 *10* 254-256

HENRY C E DARROW C W & BOSHES L D Psychophysiological effects of prefrontal lobotomy *Am Psychol* 1948 *3* 360

HOBER R LANGSTON M (et al) Studies on the physiological effects of non polar-polar organic electrolytes the influence of detergents upon the potentiometric reaction and the contractility of nerve and muscle *J Gen Physiol* 1948 *32* 11-20

HOEN T I ANDERSON R K & CLARE F B Metastatic brain abscess originating in the lungs treated with massive doses of penicillin *U S Nav M Bull* 1948 *48* 778 787

HORSTEN G P M Is it permitted to use myostatine in electroencephalography? *Acta brevia neerl* 1948 *15* 82

JASPER H H Charting the sea of brain waves *Science* 1948 *108* 343-347

JOST H Electroencephalographic records in relation to blood pressure changes in eclampsia *Am J M Sc* 1948 *216* 57 63

KELLOGG W N Conditioning involving the two body sides after hemidecortication *Am Psychol* 1948 *3* 237

KENNARD M A & WILLNER M D Significance of changes in electroencephalogram which result from shock therapy *Am J Psychiat* 1948 *105* 40 45

KENNEDY J L GOTTSDANKER R M ARMINGTON J C & GRAY F E A new electroencephalogram associated with thinking *Science* 1948 *108* 527-529

KENNEDY J L & TRAVIS R C Surface electrodes for recording bioelectric potentials *Science* 1948 *108* 183

KLEIN R & EARLY D F Observations in electrically-produced epileptic convulsions tonic neck and labyrinthine reflexes upon the eyes *J Ment Sc* Lond 1948 *94* 581 589

LAPICQUE L L excitabilite rythmogene et l isochronisme neuro-musculaire *Arch neerl physiol* 1948 *28* 377-384

LEVIN S & GREENBLATT M Electroencephalogram in cases with cortical atrophy and ventricular dilatation *Am J Psychiat* 1948 *105* 220 223

LEWIS N D C Cerebral topectomy *Am J Psychiat* 1948 *105* 151

LIBERSON W T Brief stimulus therapy physiological and clinical observations *Am J Psychiat* 1948 *105* 28 39

LICHTENSTEIN P E Effects of lobotomy on feeding inhibition and neurosis in dogs *Am Psychol*, 1948 *3* 360

LLOYD D P C & Mc INTYRE A K Analysis of forelimb hindlimb reflex activity in acutely decapitate cats *J Neurophysiol* 1948 *11* 455 470

LUCO J V EYZAGUIRRE C & PEREZ F Effects of amphetamine and cocaine on neuro muscular function *J Pharm Exp Ther* 1948 *93* 261 272

MALMO R B Reduction in general intelligence following frontal gyrectomy and frontal lobotomy in mental patients *Am Psychol* 1948 *3* 277

MALMO R B SHAGASS C DAVIS J F CLEGHORN R A GRAHAM B F & GOODMAN A J Standardized pain stimulation as controlled stress in physiological studies of psychoneurosis *Science* 1948 *108* 509-511

MARGARIA R The rhythm of activity of motor neurones an interpretative hypothesis of the electroencephalogram *Arch neerl physiol* 1948 *28* 399-407

MARSAN C A & FUORTES M G F Elettroencefalografia scopi possibilita e metodi *Arch psicol neur* Milano 1948 *9* 260-287

MAURO A & BLACK S P W An electronic controller of volleys in electrical stimulation *Yale J Biol & M* 1948 *20* 567-569

MEYER A & McLARDY T Posterior cuts in prefrontal leucotomy a clinicopathological study *J Ment Sc* Lond 1948 *94* 555-564

NEFF W D & YELA M Function of the auditory cortex the localization of sound in space *Am Psychol* 1948 *3* 243

NOELL W K The recovery of the brain from anoxia after administration of analeptic drugs electroencephalographic studies on rabbits *J Aviat M* 1948 *19* 337-345

NOELL W K & CHINN H I The cerebral survival time of rabbits in anoxia *School of Aviation Medicine* Randolph Field Texas *Quarterly Research Report* Oct 1948 Project #21-02-071 5-6

O LEARY J L Guide to the indications for brain wave recording *Dis Nerv Syst* 1948 *9* 263-269

PICK E P & FEITELBERG S Thermogenetic action of adrenalin and benzedrine on the brain *Arch internat pharm dyn* Gand 1948 *77* 219-225

PRAST J W & NOELL W K Anoxia warning device I The slow-wave activity of the brain during earlier stages of oxygen lack *School of Aviation Medicine* Randolph Field Texas *Quarterly Research Report* Oct 1948 Project # 21-02 050 4-5

REIMAN F Evaluation of leucotomy results *Am J Psychiat* 1948 *105* 86-89

RENSHAW B & ROSENBAUM H Respiratory pathways in the cervical spinal cord *Anat Rec* 1948 *101* 738

RICARD A & GIRARD P F De la leucotomie prefrontale unilaterale gauche au probleme des dominances cerebrales les diphrenies *Lyon chir* 1948 *43* 526-531

RICCIUTI H N A comparison of critical flicker frequency n psychotics psychoneurotics and normals *Am Psychol* 1948 *3* 276-277

ROTHERAM W An electronic method for immediate visual recording of the pulse rate *Brit J Phys M* 1948 *11* 115

ROWLAND L P & METTLER F A Relation between the coronal suture and cerebrum *J Comp Neur* 1948 *89* 21-40

RUSSELL R W PIERCE J F (et al) A new apparatus for the controlled administration of electroconvulsive shock *J Psychol Provincetown* 1948 *26* 71-82

SARNOFF S J HARDENBERGH E & WHITTENBERGER J L Electrophrenic respiration *Science* 1948 *108* 482

SCHIFF E DUGAN P KENNARD M A & WELCH L Effects of pathological anxiety in childhood on EEG and conditioned PGR *Am Psychol* 1948 *3* 371

SCHNEIDER G L electroencephalographie *Schweiz Bl Krankenpfl* 1948 *41* 192

SCIARONI G H Reversal of circulation of the brain partial reversal in four humans treated for paralysis and mental conditions *Am J Surg* 1948 *76* 150 164

SHANES A M & HOPKINS H S Effect of potassium on resting potential and respiration of crab nerve *J Neurophysiol* 1948 *11* 331-342

SPEIDEL C C Growth of nerve fibers as revealed by fast motion cine-photomicrography *Anat Rec* 1948 *101* 697

SPIEGEL E A Progress in neurology and psychiatry an annual review New York Grune Stratton 1948 *14* 661 pp

SZENTÁGOTHAI J Anatomical considerations of monosynaptic reflex arcs *J Neurophysiol* 1948 *11* 445-454

TASAKI I & FUJITA M Action currents of single nerve fibers as modified by temperature changes *J Neurophysiol* 1948 *11* 311-315

TASAKI I & MIZUGUCHI K Response of single Ranvier nodes to electrical stimuli *J Neurophysiol* 1948 *11* 295-303

TASAKI I MIZUGUCHI K & TASAKI K Modification of the electric response of a single Ranvier node by narcosis refractoriness and polarization *J Neurophysiol* 1948 *11* 305-310

TOWER D B & McEACHERN D Acetylcholine and neuronal activity in craniocerebral trauma *J Clin Invest* 1948 *27* 538

TOWLER M L Clinical value and limitations of electroencephalography *Texas J M* 1948 *44* 349-354

WARD A A Jr McCULLOCH W S & KOPELOFF N Temporal and spatial distribution of changes during spontaneous seizures in monkey brain *J Neurophysiol* 1948 *11* 377-386

WARD A A, Jr McCULLOCH W S & MAGOUN H W Production of an alternating tremor at rest in monkeys *J Neurophysiol* 1948 *11* 317-330

WEIL A A Neurophysiological disturbances following electric shock therapy electroencephalographic observations *Ohio M J* 1948 *44* 1017

WEYDEN J B van der Post-traumatische amnesie en electroencephalographie *Geneesk gids* 1948 *26* 325

WHEELER E T & KOSKOFF Y D Certain aspects of personality as related to the electroencephalogram *Am Psychol* 1948 *3* 278

WHITE J C LIU C T & MIXTER W J Focal epilepsy a statistical study of its causes and the results of surgical treatment epilepsy secondary to cerebral trauma and infection *N England J M* 1948 *239* 1-10

WULFF V J The electrical response of frog eyes to prolonged illumination *J Cellul Physiol* 1948 *32* 31-43

WULFF V J & FREYBURGER S W Relation between the resting and action potential in the frog eye *Anat Rec* 1948 *101* 665

AUTHORS' INSTRUCTIONS

STYLE

Authors submitting manuscripts to the editors are reminded to kindly keep in mind the desirability of CLARITY BREVITY CONSISTENCY and ACCURACY Good scientific literary style is direct and to the point Ambiguous obscure or too highly specialized expressions or terms should be particularly avoided in a journal of this type which is attempting to cross barriers of language and diverse scientific and medical specialities New or esoteric terms should be carefully defined for the benefit of readers who may have difficulty in understanding either due to nationality or training

Reports of original research should generally be organized according to the following plan

(i) *Introduction* stating the object and scope of the investigation with a brief history of the subject

(ii) Technique or Methods and *Subjects or Materials* should be presented concisely in small print

(iii) *Results* with illustrative protocols sample records tables and curves or diagrams

(iv) Discussion giving *concise* interpretation of results and their special or general significance

(v) *Summary or/and Conclusions* preferably enumerated

(vi) *Acknowledgments* (in small print)

(vii) *Legends* for figures enumerated

(viii) *Illustration* lettering clear and complete should be enumerated with author s name on reverse side Originals or good photographic copies may be submitted preferably not excessively reduced Illustrations should be kept to a minimum since the cost of a large number of expensive illustrations will have to be shared by the authors

COPY

The manuscript should be preceded by a separate title page giving the complete title (all caps) the names and initials of author or authors and the name and address of the institution or laboratory where the work was done On a second separate page should appear a *running title* not exceeding 40 letters in length together with the name and exact complete address to which the proofs are to be sent Other instructions to the printer may be included on this page

All manuscripts should be distinctly typed with one *original* and one *first carbon copy* sent to the editors to facilitate distribution to the referees A margin of at least 3 cm should be left all around Typing should be *triple spaced* for parts to be printed in standard type and *double spaced* for those parts to be printed in small type Use *separate pages* for all copy in small type Footnotes should be typed single space numbered in sequence and inserted in the text immediately following the sentence of their reference

Authors are requested to try to make their copy *letter perfect* throughout to ease the burden of the editorial staff Authors will be charged for all corrections on the proof arising from errors or changes in the original manuscript

TABLES AND FIGURES

Numerical data presented in tabular form should be typed on a separate page for each table Consecutive tables should be numbered in roman numerals (I II etc) and referred to in the text by these numerals Figures (which includes sample records and graphic illustrations) should also appear each on a separate page and numbered consecutively in arabic numerals (1 2 etc) and referred to in the text by these numerals If original illustrations are sent it is wise to send a photographic copy as well to avoid further mailing of the originals

REFERENCES

Verification of references is entirely the responsibility of the author Every reference should be verified by the original source after it has been transcribed checking details of *spelling* (especially accents) punctuation authors names and complete initials complete title journal with correct abbreviation according to A WORLD LIST OF SCIENTIFIC PERIODICALS year volume and pages (first and last)

Citation of references in the text should be by author and year e g (Cannon 1925) or (Brink and Bronk 1935) or (Davis et al 1940) Citation by numbers will be used only for review articles containing a large number of references

Arrangement of list of references at end of text should be in alphabetical order of first author If

more than one he rhythm of the same author they should be in chrono tative hyper Form of citation for *journals* is indicated by the following example

SHERRINGTON C S Decerebrate rigidity and reflex coordination of movements *J Physiol* 1898 22 319-322

for books

MAGNUS R Korperstellung Berlin J Springer 1924 740 pp

Authors names should be in capitals with all initials followed by title journal (abbreviated) underlined once year volume (arabic numerals) underlined once initial and final pages (For list of abbreviations commonly used in neurophysiology see *J Neurophysiol* 1939 2, 89-99)

ACCEPTANCE OF PAPERS

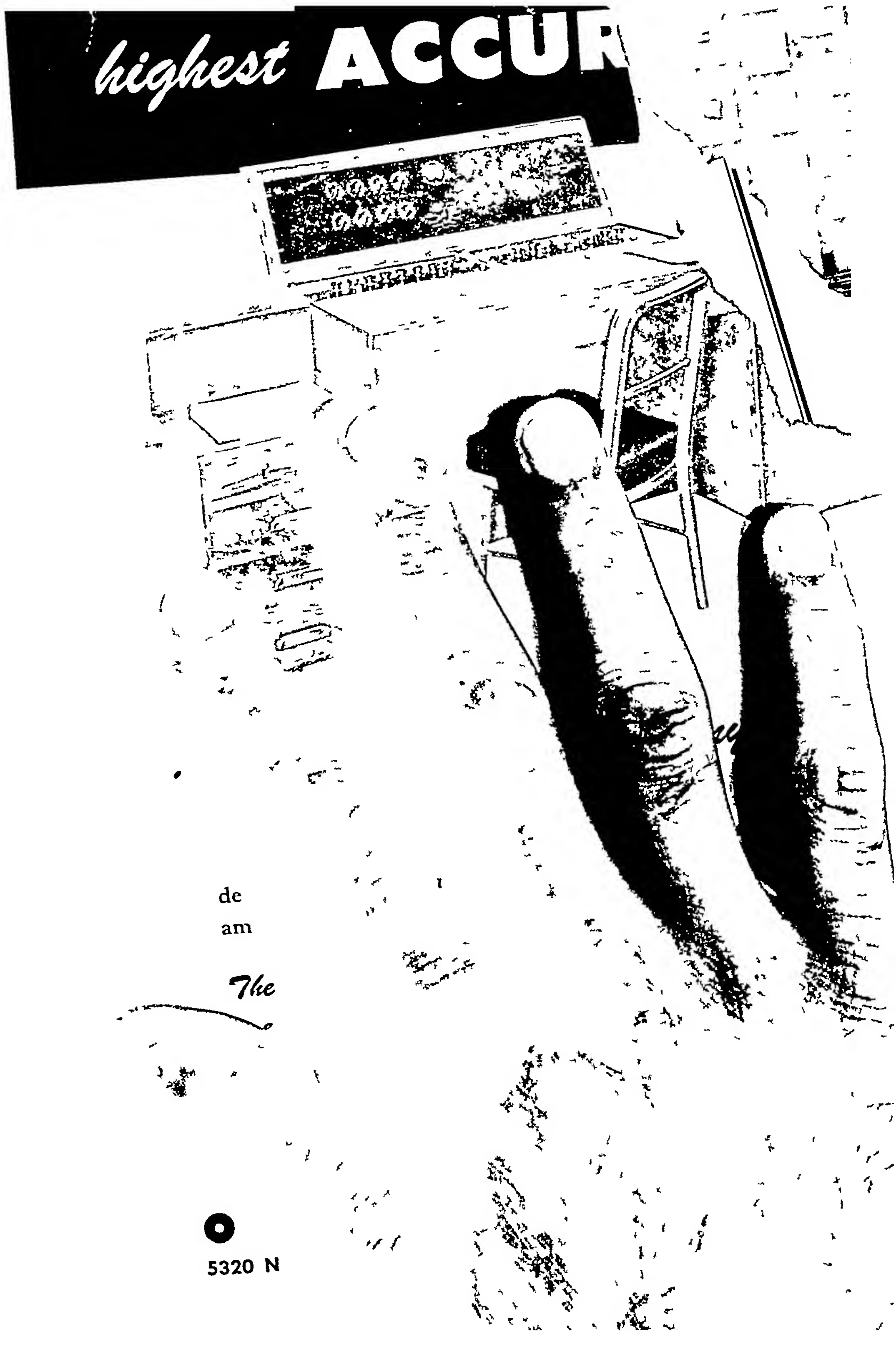
Each manuscript when submitted either to the editor or co-editor is first reviewed by him and then sent to *at least two* other members of the editorial board for a critical opinion or to other referees specialized in a particular subject Their opinions are sent independently directly to the editor or co-editor In the case of suggested revision or rejection explanation of reasons will be sent the author upon return of his manuscript Manuscripts accepted by the co editor (Dr Grey Walter) and his European editorial board will be automatically accepted by the editor (Dr Herbert Jasper) and the American and Pacific editorial board each acting autonomously

COMMENTARY

Short comments or criticism of published manuscripts journal policy interesting isolated observations suggestions or reports on research developments clinical comments news of new laboratories changes in personnel requests for assistance or applications for positions etc are solicited for this section of our journal

SOCIETY PROCEEDINGS

The proceedings of various EEG Societies throughout the world with English translations when in another language will be published as promptly as space permits Abstracts of communications presented before *Annual meetings* of national societies or before the *International Congress* should not exceed 250 words with an additional 100 words allowed for discussion Abstracts of major symposium papers should not exceed 500 words Abstracts of papers presented before regional society meetings and quarterly meetings of national societies should not exceed 150 words Proceedings should be carefully edited first by the respective Society Secretaries and mailed directly to Dr John Knott University of Iowa Iowa City Iowa U S A


highest ACCUR
de
am
The
5320 N

"THE EEG JOURNAL"

ELECTROENCEPHALOGRAPHY and CLINICAL NEUROPHYSIOLOGY

Official Organ of the International Federation of EEG Societies

This Journal was inaugurated in June, 1947, by the Executive Committee of the International E E G Organization at their first meeting in London Its purpose is threefold, to provide an official organ for the various EEG Societies being established throughout the world, to bring together in one publication selected studies of merit in the growing field of neurophysiology as applied to the understanding of human behaviour, both normal and abnormal, and to foster international cooperation and understanding among scientists with these common interests

Studies of the electrical activity of the brain provide the central theme of this Journal Its scope, however, is far broader, to include any aspect of the physiology of the nervous system or neuromuscular system which may contribute to progress in our understanding of the neural basis of behaviour Studies relating to disorders or diseases of the nervous system will be of particular though not exclusive, interest

Each Annual Volume will contain approximately 500 pages of scientific material This will appear in quarterly issues The text of each communication will be published in the English, French or Spanish language Abstracts, not to exceed 1000 words, will appear in English, if the text is in French Authors are requested to submit manuscripts in the language of their choice for publication, preferably in English since the larger proportion of our readers are more familiar with this language Abstracts should be submitted in the language most familiar to the author, to be translated by the editors when necessary

Manuscripts will receive prompt publication following their acceptance In most cases, the delay will not be more than 3 months As a rule authors will be given the privilege of withdrawing their manuscripts if they cannot be published within 6 months of their acceptance

Authors instructions for the preparation of manuscripts are given in the first issue of this Journal Papers should be concise, with a brief Introduction, followed by Technique, Results, Discussion or Interpretation, and a Summary, which may be the same as the Abstract if the author chooses Citations to literature should be by author and year, arranged in alphabetical order, appearing at the end of the text Full references must be given as follows

HARVEY H N and SMITH, J The Anatomical Basis of the Alpha Rhythm EEG Clin Neurophysiol, 1949, 1 200-220

MANUSCRIPTS from the Americas, the Pacific and Far East
to Dr Herbert H Jasper, Editor
3801 University St, Montreal 2, Canada

From the British Isles, Europe, Africa, Middle East and U S S R
to Dr Grey W Walter, Co-Editor
The Burden Neurological Institute, Bristol, England

SOCIETY PROCEEDINGS to Dr John R Knott
Psychopathic Hospital, U of Iowa, Iowa City, Iowa

TECHNICAL NOTES
to Dr Geoffrey Parr, 68 Compton Road London England
or Dr E J Baldes, The Mayo Clinic, Rochester, Minn, U S A

SUBSCRIPTIONS and ADVERTISEMENTS
to Dr Robert S Schwab Managing Editor
Massachusetts General Hospital, Boston 14, Mass

Annual subscription rate is eight dollars ($8 00) payable in United States or Canadian currency A reduced price is given to subscriptions paid through E E G Societies

GRASS INSTRUMENT CO
101 OLD COLONY AVE
QUINCY MASS
PR3-0002

February 1, 1949

To the Editors and Readers of
The Journal of Electroencephalography and
Clinical Neurophysiology

We extend our congratulations to the Editors on the inauguration of this Journal devoted exclusively to Electroencephalography and Clinical Neurophysiology. This venture will provide an international facility for the exchange of information which deserves everyone's support, financial and otherwise, to guarantee the Journal's lasting success.

The Journal can count on the support of our organization which itself has devoted the last fourteen years exclusively to instrumentation of Electroencephalography and Electrophysiology for international use.

For us the Journal is a medium for advertising our products, for maintaining close customer relationships, and for contributing our ideas and information for the improvement of techniques which in the past had to be done by correspondence and discussion.

Very truly yours,

GRASS INSTRUMENT COMPANY

Albert M. Grass

Ellen R Grass

MAKERS OF ELECTROENCEPHALOGRAPHS AND
ELECTROPHYSIOLOGICAL INSTRUMENTS SINCE 1935

GRASS INSTRUMENT CO

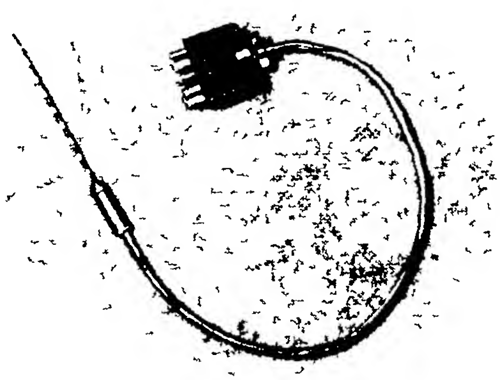
101 OLD COLONY AVE

QUINCY MASS

PR3-0002

S P E C I A L   D E V I C E S

During the years spent in the development of Electroencephalographs and Electrophysiological instruments, Grass Instrument Company has acquired the extensive facilities, the expert craftsmanship, and the engineering "know-how" needed to produce economically in quantity the special technical devices for this field. Below is a typical example of such a project.



Depth Electrode

Developed in conjunction with Dr. Frederic A. Gibbs of the University of Illinois.

The Electrode is used in the investigation of electrical activity at various depths in the brain during operation. It is a probe two millimeters in diameter with ten contacts. Can be sterilized in autoclave.

MAKERS OF ELECTROENCEPHALOGRAPHS AND ELECTROPHYSIOLOGICAL INSTRUMENTS SINCE 1935

SYMPOSIUM

PHYSIOLOGICAL BASIS OF EPILEPTIC DISCHARGE

Commission

Ralph W Gerard *Chairman*
Detlev Bronk
Earl Walker
Wilder Penfield

Speakers

Wilder Penfield
Herbert H Jasper
Warren McCulloch
Chester W Darrow
Detlev Bronk
K A C Elliott
James E P Toman
William G Lennox
Ralph W Gerard

ANNUAL MEETING

American Electroencephalographic Society
Atlantic City

June 1948

OPENING REMARKS

Ralph W Gerard, M D, Ph D
Department of Physiology, University of Chicago

I should like to take my prerogative as Chairman to introduce the symposium along the lines of Dr Jasper's presidential address last night We were complaining to each other before that meeting, that the questions which had agitated the workers in this field *in the pioneer days of long long ago* (all of fifteen years !) did not seem to be much in the forefront these days — not because they had been solved but because they had become neglected There has been a trend it seems to me, to look at records of the electrical activity of the brain which constitute the main stock in trade of electroencephalographers in the manner of the classical structural anatomists We find ourselves examining these wiggles which constitute some sort of an entity structurally — they are long or short frequent or slow sharp or round — rather than seeing them dynamically and functionally and remembering that they are but an index of processes and functions

I think the history of thought about convulsive or epileptic problems has shown the same trend, only fortunately in reverse originally the problems were mainly those of localization — where does the phenomenon start ? In recent years more dynamic questions are being asked — what is happening ? How does it come about ? What are the mechanisms ?

If we think of the problems of the nervous system as the physiologist and neuroanatomist are doing more and more today, as problems of *how* rather than of *where* things happen recognizing fully that the "where" is a necessary but not a sufficient condition of understanding then that most dramatic manifestation of neural action the *tremendous over-activity seen in convulsive* discharges, should serve, to focus the organizational the chemical, the electrical, and the physiological approaches to neural problems The present and future hopes for handling convulsions are similarly the hopes for understanding neural action

This symposium was planned for today along such lines of thought not by myself alone, as Dr Jasper indicated last night but by several others one of the most useful being Jasper himself The speakers have not had a chance to talk to each other Some have not been able to give discussants manuscripts and each is perhaps not entirely sure of his role in the total picture but I have such confidence in the men as individuals as to anticipate a thoroughly coordinated program If there is time at the close of the formal presentation and I very much hope there will be we will solicit free discussion from the floor Dr Wilder Penfield as speaker and Dr Herbert Jasper as discussant both of Montreal, will open the symposium by considering The Functional and Electrical Responses of the Brain to Epileptic Discharge

EPILEPTIC MANIFESTATIONS OF CORTICAL AND SUPRACORTICAL DISCHARGE[1]

Wilder PENFIELD, M D , F R S
Montreal Neurological Institute

The validity of the Jacksonian conception of an ictal ganglionic discharge has been verified by the clinical use of the electroencephalograph But the disturbance of electrical rhythms of the brain during a seizure is only one of the manifestations of an attack It does not tell the whole story of epilepsy The clinical picture is also important and we must enquire into the pathological cause

In opening a symposium of this type attention may well be directed to the conception that in clinical epilepsy seizures begin with ganglionic discharge in some specific location within the brain, and this applies to all types of case Since the nature of cause and the site of origin of discharge vary a plan of classification will be outlined before consideration of the nature of cortical responses to epileptic discharges

The attempt to classify cases of epilepsy on electroencephalographic evidence alone under such headings as petit mal grand mal and psychomotor was useful but it had certain drawbacks It tended to stop the study of a case before it was completed From a practical clinical point of view only the petit mal subdivision is useful

A CLASSIFICATION

Thanks to the pioneer work of Gibbs Davis and Lennox (1935) an expert is now able to recognize a three per second rhythm as characteristic of idiopathic (essential genetic) epilepsy Bursts of such rhythms accompany the minor lapses of consciousness which have been called petit mal But such lapses may develop into major generalized convulsions With this generalization the electrogram changes from bilaterally synchronous three per second waves into a bilateral discharge of rapid spikes You may call this grand mal if you like but the electrographic picture does not differ from that recorded during a generalized convulsion in symptomatic epilepsy

Consequently grand mal both clinically and electrographically is not a subdivision of the epilepsies It describes the end result of a seizure which may have begun with bilateral three per second rhythms with bilateral six per second rhythms or with spike discharges localized to one of the various areas of the cerebral cortex

It would be quite free of confusion to subdivide cases of idiopathic epilepsy (or if preferred genetic cryptogenic or essential epilepsy) into those in which only petit mal attacks appear or only grand mal or both petit mal and grand mal seizures In other forms of epilepsy the small attacks may be called minor and the larger attacks major seizures

The disturbance of electrical rhythm is maximum in the midfrontal region and appears simultaneously as a reversed (mirror) image in the midfrontal region of the other side There is good evidence to believe that the origin of these widespread discharges is to be found in diencephalon and mesencephalon[1] (Morison and Dempsey 1942 Penfield and Jasper 1947 Jasper and Fortuyn 1947) This is the distinguishing characteristic of idiopathic epilepsy

The epileptic attack may be considered a symptom of the discharge that is occurring in the gray matter or it may be looked upon as a symptom of the pathological condition

[1] From the Department of Neurology and Neuro surgery McGill University, and the Montreal Neuro logical Institute Reprint no 284

[1] These areas of gray matter are commonly referred to as subcortical in position But from a functional point of view they are *supracortical* They represent a level higher in the scale of functional representation than the cortex This explains the reference in the title of this paper to cortical and supracortical discharge

which is the cause of that discharge But classification of the epilepsies should serve the clinician as guide to therapy and to prognosis To that end we should seek in a classification to indicate first the site of initial epileptic discharge and secondly its cause

The search for cause compels the clinician to go farther Idiopathic epilepsy would seem to be due to an abnormality of cerebral physiology which has, at least, as much of a genetic background as migraine Focal cerebral seizures are produced by abnormality within some area of gray matter usually the

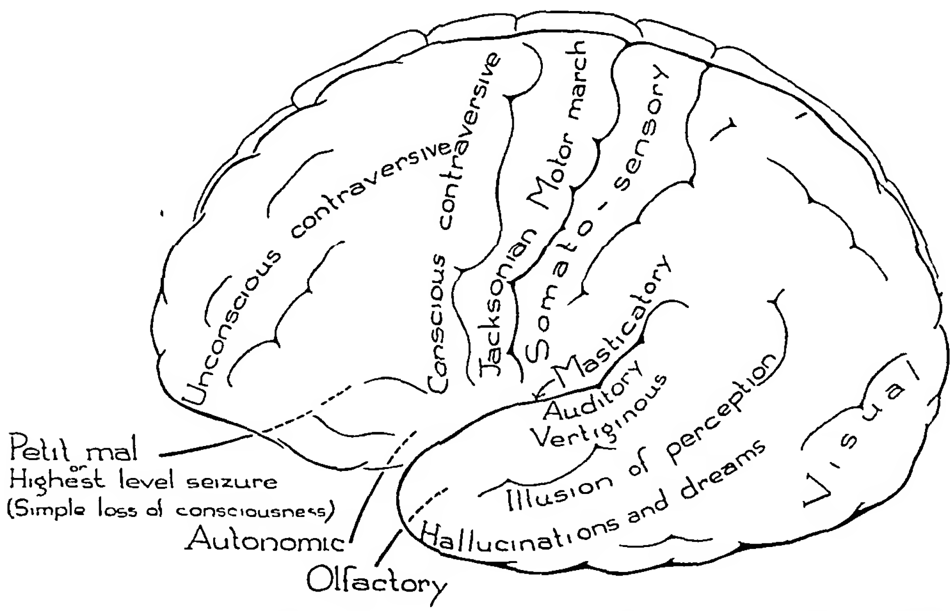


Fig 1 Patterns of seizure onset in relation to the site of origin of the epileptic discharge which produces each (PENFIELD 1948)

No useful purpose is to be served by dropping the term epilepsy but it may well be reserved for patients who suffer from idiopathic epilepsy Until the type of seizure is identified we find it useful to employ the term cerebral seizures (Table I) Study of seizure pattern and of electroencephalogram will then make it possible to withdraw from this group the cases identified as idiopathic epilepsy and the cases of focal cerebral seizures

TABLE I

CLASSIFICATION

I CEREBRAL SEIZURES
  CAUSE
II FOCAL CEREBRAL SEIZURES
  LOCALIZATION
  PATTERN
  CAUSE
III IDIOPATHIC EPILEPSY

cortex The abnormality is a continuing state affecting the ganglion cells It seems to be associated with local decrease in the amount of oxygen that reaches some portion of the area in question The cause of this change may be compression due to an expanding lesion such as tumor or abscess It may be laceration of cortex due to trauma and followed by contracting scar It may be the shrivelled gyrus that was partially destroyed by natal ischemia or by cerebral vascular accident

In the search for the exact location of the initiating discharge one must examine the pattern of the beginning of the seizure or of the minor attack whether this is sensory motor or psychical This provides us with the first clue to the localization of the focal discharge The situation of an electrographic 'spike' focus on the surface of the scalp also has great localizing value if we

allow for the possibility of error in the projection from cortex to scalp an error that will not usually be greater than 2 or 3 cm if the focus lies on the convexity of the hemisphere

A case which has been identified as one of focal cerebral seizures may be further classified as to cause location and pattern of attack (Table I) Thus a patient with Jacksonian motor seizures might receive the following diagnosis — *Focal Cerebral Seizures* localization — *right precentral* pattern — *somatosensory* cause — *birth injury* Reference to figure 1 summarizes a few of the other common seizure patterns in relation to their cortical localization Thus another patient who complained of a strange sense of familiarity (deja vu phenomenon) followed by automatism might be classified as *Focal Cerebral Seizures* localization — *right temporal* pattern — *psychical illusion* and *automatism* cause — *brain tumor* Another who became unconscious and was then observed to turn around to the right before falling in a generalized seizure might be classified as follows *Focal Cerebral Seizures* localization — *left anterior frontal* type — *unconscious adversive* cause — *unknown*

The initial EEG interpretation may give clear evidence of genetic epilepsy or it may discover a circumscribed spike focus but often conclusion must be postponed for later study It will be necessary to leave some patients in the classification of cerebral seizures (Table I) cause unknown or cerebral seizures cause — hypoglycemia and so on

It is obvious that the work of sorting out the patients who complain of seizures calls for combined clinical and electroencephalographic study, and such study has already led to new and exciting advance in our knowledge of human neurophysiology

B CORTICAL RESPONSES

The response elicited from the cerebral cortex as the result of spontaneous local epileptic discharge can be initiated in most areas of the brain by electrical stimulation There is one major exception to this statement Curiously enough stimulation of the anterior frontal region rarely produces a seizure although spontaneous seizures begin there as they do elsewhere

There is a great variety of response when different areas of cortex are activated as shown by the partial outline in table II The movement produced from the Rolandic convolutions and the sensation from there and from the other sensory areas are positive phenomena but they are very elementary in character, no skilled action and no complete picture no words no music Discharge in the elaboration areas such as those for speech produces only arrest of skilled movement It produces aphasia not speaking

TABLE II

Some Results of

CORTICAL ACTIVATION

1 MOVEMENT — Somatic
2 SENSATION — Somatic Visual Auditory Olfactory Vestibular
3 ELABORATION ARREST — Speech and other Skills
4 PSYCHICAL HALLUCINATIONS AND ILLUSIONS
5 CONFUSION OF THOUGHT AND UNCONSCIOUSNESS
6 MISCELLANEOUS — Looking Forced thinking Autonomic Phenomena etc

In the temporal cortex the response is both positive and elaborate Here well-formed hallucinations of sight and sound are occasionally produced — memories dreams and perceptual illusions

In the anterior frontal region the result of discharge is again negative An attack arising here may produce initial confusion in thinking that is detectable by an observer but of which the patient is not aware The confusion is followed by turning and loss of consciousness

Local Fits

Electrical and epileptic stimulation may or may not have a positive effect but it invariably has some negative effect although it may not always be easy to demonstrate its

nature The negative effect is explained by the fact that the area stimulated is paralyzed for its normal uses during the ictal discharge and during the immediately succeeding period of post-ictal exhaustion But it is often true that the effect of the stimulation can only be discovered if the patient is called upon to do something that depends on the function of that area during the paralysis

Some responses depend upon what may be called inborn neuronal patterns Others depend on acquired synaptic patterns It is obvious that motor phenomena which result from stimulation of the central cortex are inborn They are the same from individual to individual The order is invariable The extent of representation seems to be in proportion to the functional uses to which the parts are put by the adult But the responses to stimulation are the same in infancy and maturity

Stimulation of the motor cortex produces those movements of which the newborn human infant is capable e g simple extension and flexion of arm and leg with no delicacy of coordination but it also produces coordinated movements of vocalization of mastication sucking swallowing Similar skilled movements e g crying and feeding we bring with us into the world We are originally expert only in the arts of protest and self satisfaction The precentral gyrus is essential to the performance of the skilled movement acquired later in life and yet there is no change in the result of this form of artificial stimulation before and after the acquisition of skills

The same is true of the sensory areas of the cortex In the central cortex discharge produces only a sense of tingling or of movement in hand foot, tongue, etc , in the occipital cortex gross lights shadows colors in the first temporal convolution the simplest of sounds, in the uncus distasteful odor The quality of odor perceived may have changed little during ontogenetic development but visual and auditory perceptions have become greatly elaborated Nevertheless the evidence of that elaboration is not found in the sensory areas of the cortex

In all these sensory and motor regions we find no evidence that epileptic discharge is capable of activating acquired neurone connections But in the cortex of the temporal lobe and extending back into parietal and occipital regions a little, there are synaptic patterns which must constitute the record of previous experience, the records of memory established in duplicate in comparable areas of the two sides

In this portion of the cortex spontaneous epileptic discharge may cause the patient to see or hear things which, like his own memories exist for him but for no one else It is a psychical' experience (to borrow a word employed by Jackson) rather than a sensory one The elements of the hallucination are drawn from the patient s own memory records which are obviously laid down in that portion of the cortex The cortical record has lost its elementary character It corresponds with the perceptions of the individual and has added to it the individual s own reactions to the sight and the sound

Stimulation of the temporal cortex of a patient who has had no epileptic hallucinations does not produce one although he may say that it changes his 'thinking' or that he seems far away On the other hand when a certain hallucination has previously constituted the patient's minor seizure then stimulation may likewise produce that dream or a modification of it

Aside from the anatomical and physiological significance, these differences should throw light upon the nature of spread of the epileptic discharge Let us consider an active epileptogenic focus in the sensorimotor thumb area It gives evidence recorded in the electrogram of brief independent discharges between attacks and without producing clinical symptoms Periodically this inter-ictal fire gains sudden headway and the patient is aware of tingling in his thumb He is having a minor seizure comparable to the petit mal of the idiopathic epileptic The characters of these two minor seizures differ greatly because of the difference in the function of the gray matter where the fire is burning

Let us suppose that the discharge that is going on in the thumb area is sufficiently intense to cause it to spread A Jacksonian march is then set up into contiguous cortex and the patient máy begin to feel a tingling in his face in addition to that in his thumb The pattern of that cortical spread is not determined by any particularly close functional relationship that exists between the thumb and that side of the face It is determined merely by the fact that, anatomically, the sensory representations of face and thumb lie next to each other

Now let us compare with this the probable mechanism of a psychical hallucination As discharge in a temporal focus flares up it seems to set off activity in certain ganglion cells *which are scattered over the temporal* region but which are bound together in a synaptic pattern

The activity thus artificially produced in this pattern causes the patient to be aware of an experience which he is apt to say is like a dream He hears and sees people carrying out action The elements of the hallucination are derived from his own memory for his mother or his friends may be there in familiar surroundings yet he recognizes that this is different from a memory that he would himself summon It is obvious that the discharge of the epileptogenic focus has activated an acquired neurone pattern not an inborn one

In such a case the stimulating electrode may also activate the same hallucination when the cortex is exposed Action goes forward as in a dream until the electrode is withdrawn, when the hallucination may vanish without evidence of after discharge Likewise if the electrode is applied to the proper point on the postcentral gyrus a sensation may be produced *in the thumb* It continues while the electrode remains in place *and stops on its* withdrawal

In the one case a sensory phenomenon is being produced in the other a psychical phenomenon The pattern in the temporal cortex is selected by the excitation only because previous facilitation has made it dominant It is only one of a great many possible neurone patterns in which are filed away the *experiences of an individual* But the whole ganglionic mantle is not involved in epileptic discharge during the hallucination It is the nature of memory that movement may go forward in it This does not mean epileptic spread but may apparently be produced by stimulation that remains local

However if the epileptic discharge that is localized to one area of temporal cortex during the production of a hallucination should begin to spread, it would do so into contiguous areas of cortex Then it seems likely that the hallucination would come to an end It would be crowded out as other phenomena make their appearance

Discharge within the temporal cortex may also produce illusions The things that the patient is looking at the sounds that he hears the position of himself in regard to his environment may seem to him to be strangely altered These are illusions of perception He feels that he has experienced it all before (deja vu' phenomenon) or that it is absurd or things are far away or suddenly near or he himself seems to be far away in space and to be observing himself He is not unconscious of course and he maintains an awareness of the reality of things as well as of this distortion of his own perceptions He is even then using his memory records for he makes a judgement by comparing the present perception with what his memory tells him he should expect

Hughlings Jackson with whimsical insight called this state of double consciousness — mental diplopia Even during a hallucination the subject is usually dimly aware that he is dreaming

It is obvious therefore that the temporal cortex and some adjacent cortex serve the uses of memory recording for the hallucinations are made up of remembered experience and inasmuch as the patient later remembers the details of the hallucination it is possible that he employs the other temporal cortex for the purpose But if the attacks that involve the temporal region (and also those

of the island of Reil) spread further the subject is apt to become amnesic He may even have a retrograde amnesia that expunges the memory of his preceding hallucination or illusion

Such a patient might remember a smaller attack of let us say illusion after it was over But after a larger attack he would not recall the initial illusion although he may have indicated to an observer that he knew an attack was starting During the amnesia it seems likely that the central portion of the memory recording mechanism is disabled by spread of the discharging state along projection pathways Such amnesia is associated with automatism

C SPREAD OF EPILEPTIC DISCHARGE

There are two kinds of spread of the epileptic discharge

1 *Spread by contiguity* We have discussed this already In the cortex the altered state creeps along the gray carpet in one direction or in another producing clinical evidence of its advance, electrographic evidence of increased potentials and marked increase in local blood flow It may thus pass from one cortical field into a functionally little related field

It is as though the initial focus were capable of forming a juice an Alpha substance'[1] which was capable of setting adjacent ganglion cells on fire and as though these new cells in firing poured out more substance and so the state is propagated across the surface until distant firing through projection tracts produces a generalized explosion

2 *Spread by projection* It is at once obvious that cortical areas are capable of transmitting this discharging state to areas of gray matter situated at a distance This is particularly true along the great projection pathways that connect the cortex with subcortical nuclei It would seem likely that axonal conduction of the enormous energy being released in the original focus might well overstimulate the second area through axonal pathways much as a stimulating electrode may do

D AUTOMATISM

The problem of epileptic automatism is of great importance In such a state the patient retains bodily control with little or no understanding of the meaning of things If it may be said that consciousness is present, it is certainly in a much impoverished form and he will have no memory of what takes place during the automatism

The fact that there is such a thing as epileptic automatism suggests that there is within the nervous system an area of gray matter, which is particularly related to the processes of understanding deciding and remembering It means, further that this area of gray matter may be paralyzed without arresting an elaborate system of coordination between sensation and motor control

Some degree of automatism may follow any type of generalized convulsive seizure making its appearance during the period of recovery But without preliminary major attack it occurs chiefly in seizures which arise in the temporal region It also occurs as the result of petit mal discharge and, less frequently as the result of epileptic discharge in one anterior frontal region without major convulsion For the purposes of discussion we may refer to temporal automatism petit mal automatism and frontal automatism

1 *Temporal automatism* Let us take as an example the patient who has just had the following psychical illusion He was suddenly seized with the feeling that what was happening to him had all happened before He remembered no more But those standing with the patient might have seen him swallow and perhaps salivate actively They observed that their companion had changed He was not the individual they knew but by startling metamorphosis a complete automaton capable of vigorous resistance but not open to reason devoid of understanding

The explanation of this change is that at the time of the onset of automatism, the

[1] See PENFIELD 1937

ganglionic discharge in the temporal cortex had presumably extended its influence from the cortex along projection pathways into the gray matter in the diencephalon and midbrain thus inactivating this gray matter. It is at this higher level that the neural mechanism is located which is essential to the process of memory-recording in both temporal fields. It might seem that he was for the time being cut off completely from the body of his past experience but he was otherwise capable. As the discharge spread by projection to this higher level it may have been spreading also by contiguity into Sylvian or insular cortex thus causing him to swallow and to salivate. But he remembered no more than the illusion.

2. *Petit mal automatism*. It is not always easy to differentiate between petit mal automatism and temporal automatism. In petit mal there is no warning no lesser attack that precedes the state and usually no mastication or salivation only a stare which warns the patient's friends that something has snuffed out conscious perception although he may not fall. The petit mal is usually of much shorter duration than temporal automatism. The temporal automaton is apt to wander off to a distance and to fight when attempts are made to control him. This would be rare indeed during petit mal attacks.

3. *Frontal automatism*. States of altered consciousness with confusion and stereotyped thinking or behavior may also be produced by epileptic discharges arising in anterior mesial or orbital portions of one frontal lobe. In some cases automatic behavior may result which also simulates closely that caused by discharges of temporal origin. In such cases the accompanying electrographic disturbance may resemble the slow petit mal rhythm but is not identical with it. This will be elaborated in the contribution of Dr Jasper to this symposium.

In all cases of automatism the epileptic discharge may be said to have affected the gray matter that constitutes a higher level of integration than the cerebral cortex. Discharge evidently produces local paralysis of function at that level as it does elsewhere. This highest level the seat of consciousness' is not a point. Neither is it an isolated nucleus. It is made up of parts which seem at times to be differentially inactivated.

However the conclusion with regard to the highest level which may be drawn from the above reasoning is that it includes gray matter and that it may be inactivated by epileptic paralysis without paralyzing the sensorimotor integrating mechanism. In the integrating mechanism that is still active during automatism there is an effector mechanism and a mechanism for the reception of the afferent streams of information but there is no memory-recording system. If the effector or motor mechanism is involved in discharge the patient has a generalized seizure also without subsequent memory. But he is then obviously incapable of automatic behavior except during a brief phase of the recovery from his attack.

From the electrographic point of view it would seem that in petit mal the discharge which produces automatism originates in that portion of the highest level complex which activates the three per second rhythm. On the other hand in temporal automatism there is involvement of the neuronal circuits which are responsible for the six per second psychomotor rhythm.

In each case the patient shows the negative or inactivating effect of an epileptic discharge that is occurring in a central mechanism. As in all seizures the negative or paralytic effect appears during discharge and during the immediately succeeding period of ganglionic exhaustion. Automatism therefore, is an ictal phenomenon and a post-ictal phenomenon as well.

The temporal automaton has been cut off completely from the body of his previous experience through a mechanism related to the psychomotor rhythm. His condition is not psychomotor however but *psychoparetic*. Actually in all automatism there is paresis of a portion of the highest level of neural integration and therefore all automatism may be said to be psychoparetic.

REFERENCES

GIBBS F A DAVIS H and LENNOX W G Electro-encephalogram in epilepsy and in conditions of impaired consciousness *Arch Neurol Psychiat* Chicago **1935** *34* 1133-1148

JASPER H H and DROOGLEEVER-FORTUYN J Experimental studies on the functional anatomy of petit mal epilepsy *Res Publ Ass nerv ment Dis* **1947** *26* 272-298

MORISON R S and DEMPSEY E W A study of thalamo-cortical relations *Amer J Physiol* **1942** *135* 281-292

PENFIELD W and JASPER H Highest level seizures *Res Publ Ass nerv ment Dis* **1947** *26* 252-271

PENFIELD W The circulation of the epileptic brain *Res Publ Ass nerv ment Dis* **1937** *18* 605-637

PENFIELD W The surgical treatment of focal epilepsy British Surgical Practice, London Butterworth, **1948**

ELECTRICAL SIGNS OF EPILEPTIC DISCHARGE[1]

Herbert H JASPER, M D , D ès Sc
Montreal Neurological Institute

FOCAL CORTICAL DISCHARGE

There is only one form of electrical activity which we consider pathognomonic of a *local* primary discharging lesion which may be epileptogenic This is the random spike discharge It is a rapid surface negative wave of the order of ten to twenty milliseconds duration when recorded at its source on the cortex When recorded directly at its source on the exposed brain it may reach 500 to as high as 2000 microvolts in amplitude When obtained through the skull and scalp these spikes are attenuated in amplitude and prolonged in time They appear on the scalp as aperiodic rapid waves of about twenty to forty milliseconds duration and with voltages from about 50 to 500 microvolts

Random spikes are similar in form regardless of the cortical area from which they are obtained They do not seem to depend upon the cyto-architectural structure of any given area of cortex but seem to be a surface discharge probably of only the superficial layers of the cortex when they are of small amplitude and relatively monophasic When they become increased in amplitude and contain a large diphasic component usually electropositive at the surface evidence of conduction to a distant area may be found The conducted wave recorded at a distance is temporally dispersed appearing as a sharp wave that is a wave of rapid rising phase but prolonged falling phase These sharp waves may be of 50 to 200 milliseconds in duration and they also are of the same form regardless of the area of cortex from which they are recorded In figure 1 is shown a local spike discharge together with multiple spikes from an area of cortex just above the Fissure of Sylvius Conducted waves just below the Fissure of Sylvius show the temporal dispersion which occurs with this type of conduction across a fissure in one hemisphere

To those who are familiar with the strychnine spikes which have been used to such advantage by Dusser de Barenne and McCulloch (1939) and their associates it will be seen that the spikes of the epileptogenic lesion in man are comparable in almost every respect It is surprising that their conduction along fibre tracts does not interfere to a greater extent with localization studies of the focus of spike discharge although mirror foci are occasionally seen When the spike is of superficial origin on the convexity of the cortex just beneath the skull and when it is of moderate amplitude little evidence of conduction is apparent either from the homologous area of the opposite hemisphere or from other areas of the same side If however this local spike process is buried in a fissure such as within the island of Reil or if its origin is within the longitudinal fissure or on the undersurface of the brain it cannot be ordinarily recorded from the scalp surface What is recorded then are only the conducted disturbances where they may appear as prolonged sharp waves or as rhythmic potential waves They may be predominantly from one hemisphere or perhaps bilaterally from both hemispheres as the spike process activates mechanisms firing to both sides of the brain

These hidden spike foci may be very difficult of discovery in the usual E E G examination They may be so precisely localized that they are missed in the routine E E G with a limited number of electrodes on the scalp surface or they may arise in a buried atrophic gyrus and no evidence of their presence may be seen from the scalp

[1] From the Department of Neurology and Neurosurgery McGill University and the Montreal Neurological Institute Reprint no 287

surface In many instances we have found them only when electrodes were placed directly over the buried gyrus on the exposed cortex or on the mesial or ventral surface of the hemisphere

The random spike when appearing at relatively infrequent intervals and of only moderate voltage, is scarcely ever associated with any apparent change in the patient either objectively or subjectively Changes in the patient are seen only when they begin to fire repetitively and attain a higher voltage This seems to be consistent with the necessity for summation in the activation of the cortex, since single shocks producing single responses from the cortex are also unable to produce outward signs of excitation (Adrian, 1936 and Adrian and Moruzzi, 1939)

irregular sequence that the convulsive movements of the left hand began At first this rapid firing of local spikes is disorganized but it soon becomes integrated into a regular rhythmic discharge Not until this regular rhythmic discharge develops and the process begins to spread to other areas or perhaps more probably to subcortical structures is there an effect on consciousness

Another characteristic of a focal epileptogenic lesion is the facility with which after-discharge may be induced in it following electrical stimulation This method of locating areas of cortex which seem susceptible to epileptic activity has been developed by Walker (1947) and we have recently had the opportunity of confirming this observation in a number of patients It was our first impression that the area from which

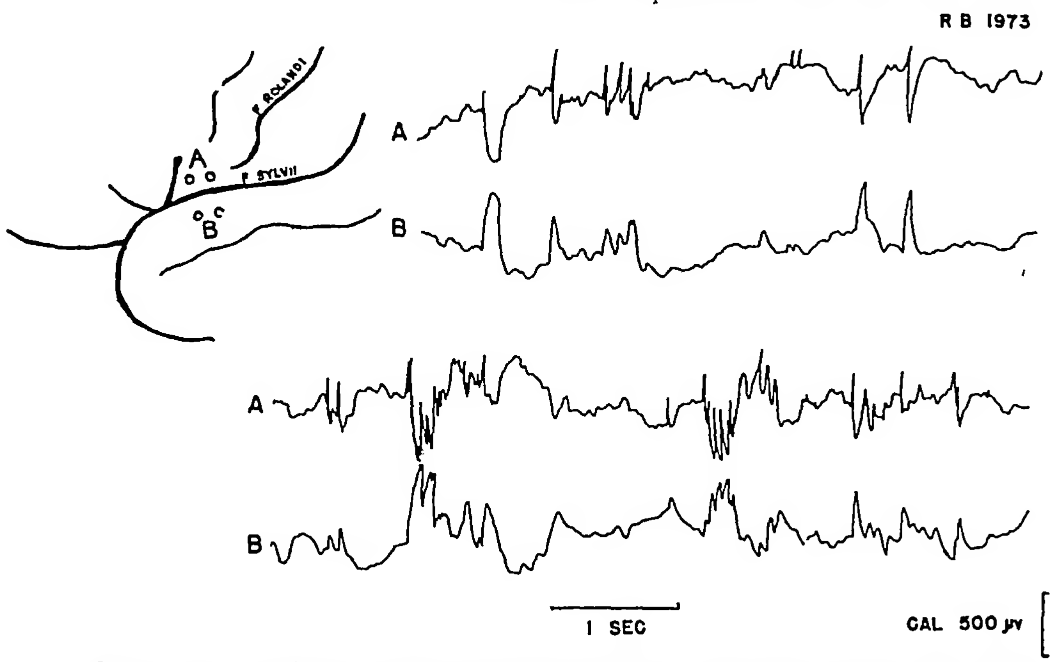


Fig 1 Random spike discharges appearing spontaneously in the electrocorticogram of a patient with focal seizures arising on the border of an epidermoid tumor The spikes arising from just above the Fissure of Sylvius at A are initially surface negative with a longer positive phase when conducted out of this local area to B across the Fissure Note temporally dispersed conducted waves in lines marked B

The development of a random spike focus into a clinical seizure is perhaps best illustrated in an example from a patient with Jacksonian epilepsy with a spike focus in the right precentral hand area As shown in figure 2 it was not until the spikes began to repeat themselves in a fairly rapid but still

random spikes were obtained spontaneously did not always correspond to the area from which after-discharge could be most readily induced following electrical stimulation However, with further study we are inclined to agree with Walker in that with most patients the area from which random spikes

are obtained is also the area from which after-discharges may be most readily induced and are seen to be of greater duration following electrical stimulation In order that with metrazol may be used when necessary but the spontaneous discharge usually present without the help of these artificial agents is most dependable

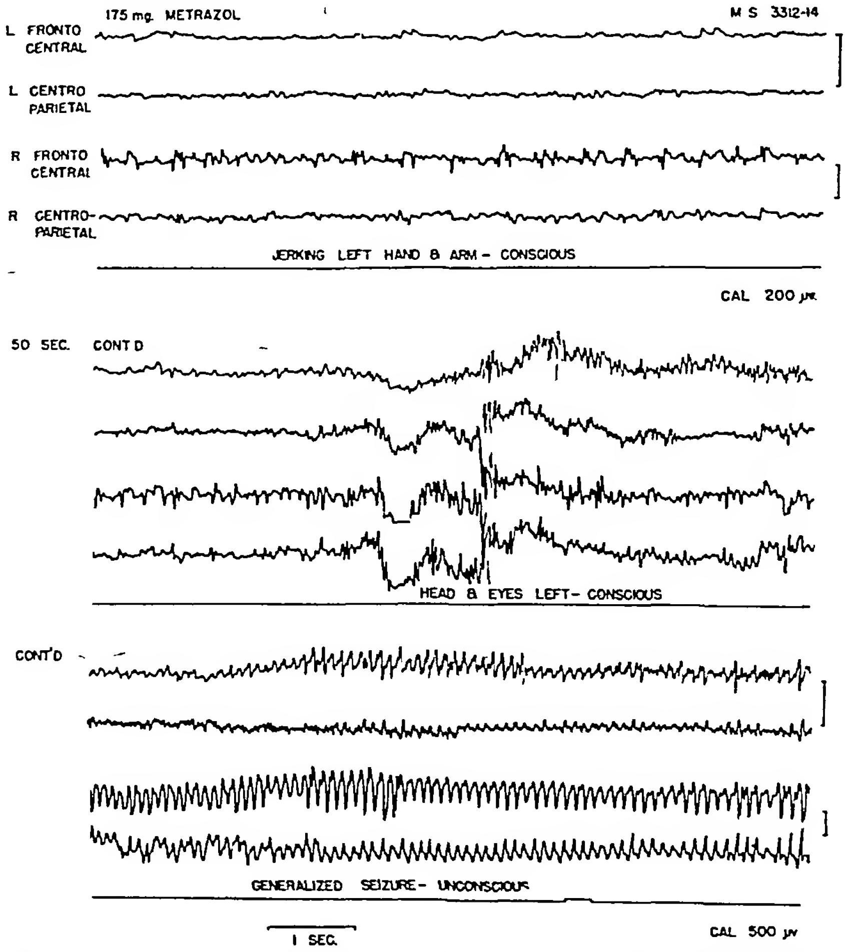


Fig 2 Jacksonian motor seizure with irregular spikes from EEG (scalp surface) over right fronto central region Further description is given in text

this method may be used however great care must be taken in establishing the constancy of the strength and duration of electrical stimulation so that all cortical areas are compared with the same amount of stimulus Otherwise errors may be introduced since after-discharge may be produced from any cortical area following sufficient stimulation We still feel that the spontaneous discharge is the most reliable indication of an epileptic focus Activation either by hyperventilation electrical stimulation or

SPREADING EPILEPTIC ACTIVATION OF THE CORTEX

It is necessary to distinguish clearly between the conduction of a local epileptic discharge over neuronal circuits such as was shown in the temporal dispersion of the spike into a sharp wave and the spread of epileptic activation to adjacent areas of gray matter These two processes should not be confused although the first may lead to the second that is initially a conduction process may finally lead to secondary epileptic

activation of the tissue which has received excessive bombardment of impulses from the primary focus

This distinction between simple conduction and the spread of epileptic activation was brought out very clearly in a series of experiments carried out in collaboration with Drs Pope and Morris (1917) in which chronic focal cortical epileptogenic lesions were produced in the motor cortex of monkeys by the alumina cream method of Barrera and Kopeloff In these animals typical random spike discharges developed in the region of the lesion and sharp waves were regularly recorded from the homologous cortical area of the opposite hemispheres During the time between clinical seizures the local spikes appeared from only a small area of the right precentral gyrus and the sharp waves from a small area in the contralateral central region Conduction of the local epileptic activation seemed most directly therefore across the corpus collosum to the homologous area of the opposite side However when an epileptic seizure developed, the spread did not occur first to the opposite hemisphere but it proceeded first to adjacent areas in the cortex on the ipsilateral side This is typical of the usual Jacksonian march The path of maximum conduction before the onset of the clinical seizure was to the contralateral area of the opposite hemisphere while the path of spread of the activation process was to adjacent areas of cortex contiguous with the initiating focus

The form of spreading epileptic activation in the cortex is quite different from the simple conduction process where single waves are transmitted to a distant area The spreading epileptic process initiates true autonomous epileptic activity in the cortex involved, continuing after the primary discharge has ceased Its first sign is an enhancement of the voltage of the existing electrical activity of that particular area with some gradual alteration in frequency This enhancement of the resting spontaneous activity occurs before this area becomes truly engulfed in the spreading wave of the epileptic process If the predominant resting activity of a given area is 10 per second the first sign of epileptic activation of this area of cortical spread may appear as high voltage rhythmic waves of 8 to 12 per second If the resting activity is previously slow the spread into that area might be described according to Grey Walter as a rising delta discharge"

An example of the appearance of a wave front of spreading epileptic activity first as a change in the background slow rhythm is given in the following patient (Fig 3) with a large meningo-cerebral cicatrix of the right frontal lobe There was a focus of spikes posterior to the scar at point A Electrical stimulation of this area started a prolonged afterdischarge which caused the patient to exclaim seizure' Soon this discharge disappeared from the recording electrodes and it was thought the seizure was over but the patient was still a little confused and restless, though responsive Then there occurred a gradual change in the delta activity anterior to the scar This change was manifest by a gradual increase in its amplitude and frequency Finally a true multiple spike discharge developed The patient was not aware that the seizure was continuing although he remained restless and asked for the urinal, but did not use it

This gives the character of one form of a spreading epileptic process first an enhancement of the background rhythm before the local process becomes sufficiently intense to produce a multiple spike pattern

In certain other cases a depression of spontaneous activity seems to precede the onset of epileptic discharge, but this seems to be a special process in only certain brain areas which perhaps have a type of 'suppressor' or inhibitory function

Electrical signs of epileptic discharge may spread over the surface of the silent' areas of the cortex with scarcely any change in the patient although effects would probably be noted if the proper psychological tests were employed For example in another patient, electrical signs of epileptic discharge were recorded from electrodes directly on the orbital surface of the left frontal lobe (wires

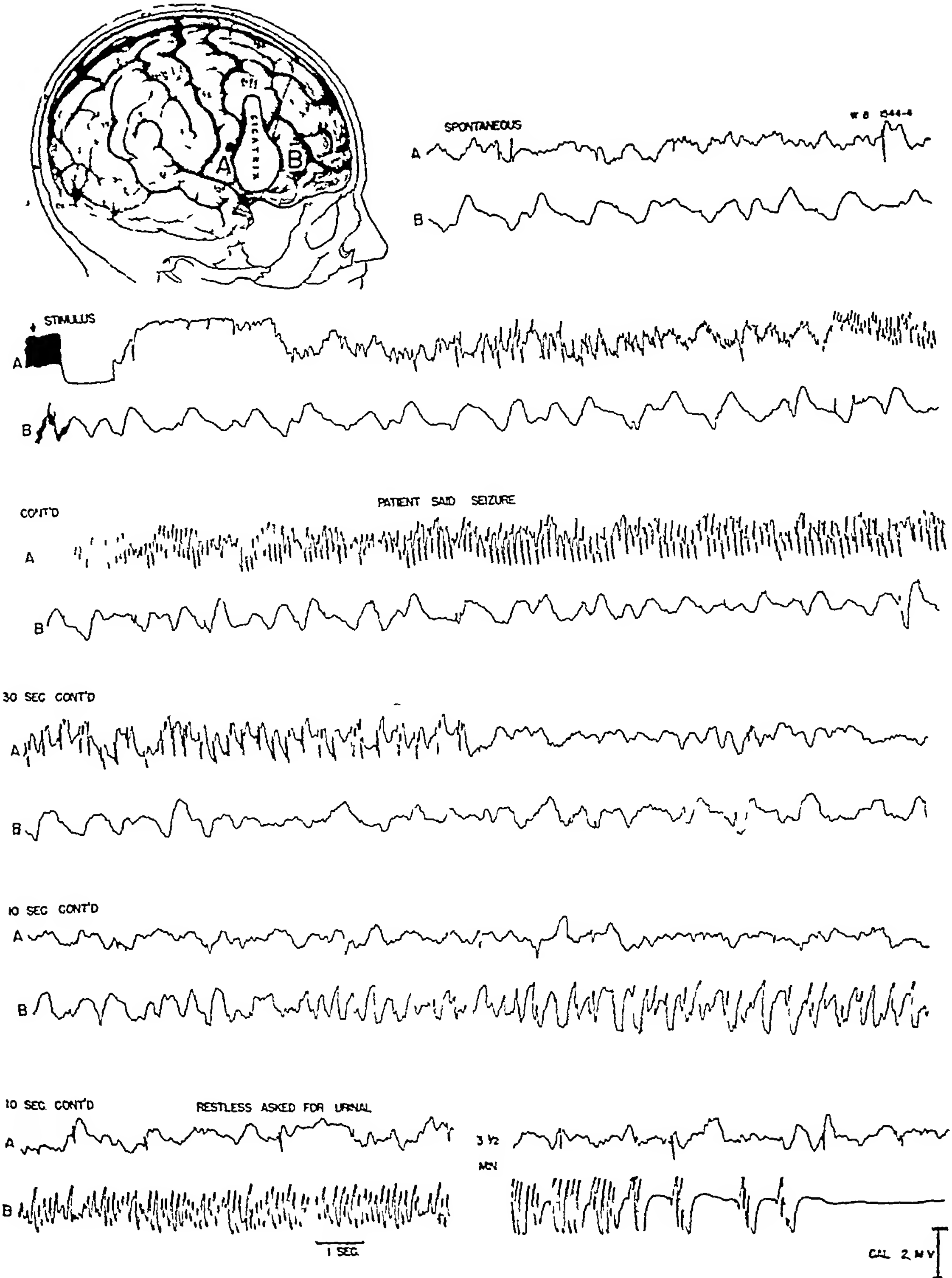


Fig 3 Electrocorticograms from pairs of electrodes placed just posterior (A) and anterior (B) to a large post traumatic cicatrix of the frontal lobe The pairs of tracings from above down are samples of records taken simultaneously from A and B After electrical stimulation near A a local after-discharge developed and stopped after about 40 seconds Twenty seconds later the delta waves at B (5th tracing) began to accelerate and become sharp followed by rapid epileptiform discharge lasting about 4 minutes during which the activity of the original focus stimulated had long since returned to its pre stimulation form

led out through a trephine hole) two minutes and forty seconds before the nurse observing the patient was aware that an attack was in progress, and she had seen many of his attacks before

THALAMO CORTICAL SYSTEMS IN RHYTHMIC EPILEPTIC ACTIVITY

A spike discharge of cortical origin may activate thalamo-cortical rhythmic systems so that large areas of the cortex sometimes bilaterally, may be involved in rhythmic activity initiated by a single focus Bilaterally synchronous rhythmic sharp waves or sharp and slow wave complexes usually repeated at 2 to 2 5 per second may result from a local spike focus on the mesial or orbital surface of one frontal lobe (Fig 4) Local epileptogenic lesions of one temporal region if situated within the island of Reil in the extension of its cortex forward onto the tip of the temporal lobe or ventrally into the uncinate or hippocampal regions commonly produce bilateral rhythmic discharges These cortical areas are apparently closely related to a central rhythmic system (possibly the fornix system) which sets up bilateral rhythmic discharges localized vaguely over fronto-temporal regions as recorded from the outside of the head The most characteristic frequency of this system is between 4 and 6 per second, although it may respond at about 2 per second as well Its frequent association with automatic behaviour has gained for it the term psychomotor ', although other systems as well particularly frontal may also produce epileptic automatisms Lennox and Brodie (1946) have shown that lesions in subcortical structures also may produce this type of electrogram, though not associated with epileptic automatisms Hence primary activation of the subcortical rhythmic system may occur as well as its activation secondary to a cortical discharge

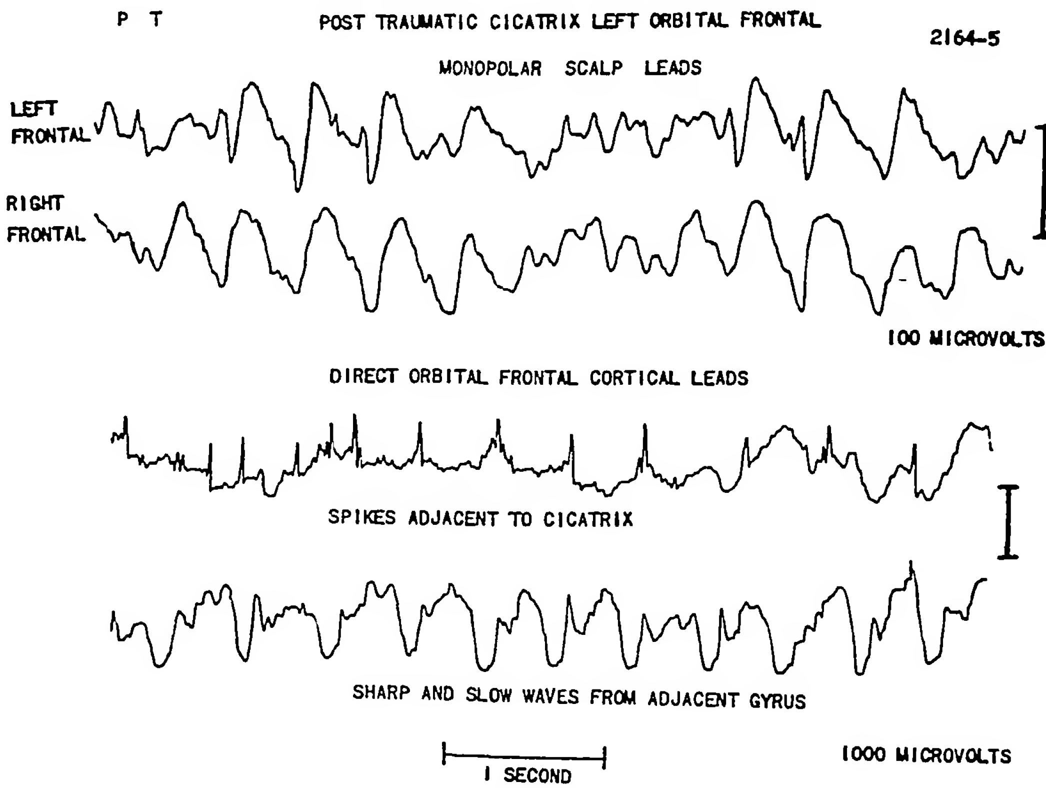


Fig 4 Electroencephalogram above shows high voltage bilaterally synchronous two per second sharp waves from left and right frontal ear linkages in patient with post-traumatic lesion with spicule of bone penetrating brain on orbital surface of left frontal lobe Electrocorticograms below show spikes obtained directly from the cortex adjacent to the lesion and sharp waves from an adjacent gyrus on the orbital surface

It has been shown in experimental studies that a single brief pulse administered to certain critical areas of the thalamus is capable of initiating a train of rhythmic waves in widespread areas of the cortex (Jasper and Droogleever-Fortuyn, 1947). Consequently it may be assumed that this brief electrical pulse may be supplied by the cortex itself and fired into the thalamus, setting off a thalamo-cortical rhythmic system (Penfield and Jasper 1947). It may not always be the thalamus involved but to our present knowledge this is the principal centre for control of rhythmic activity of the cortex.

Epileptic discharges may also be initiated from the thalamus and spread outward to the cortex. This process can not be elaborated in detail in the present communication but suffice it to say that after-discharge can be induced in the various nuclei of the thalamus and can be seen to be projected to cause a secondary epileptic activation of the cortex. Recording from the thalamus, we have seen also that the spread of cortically initiated after-discharge may also involve thalamic nuclei.

A thalamic pacemaker for the bilaterally synchronous wave and spike discharge of petit mal was established in our experimental studies with Droogleever-Fortuyn (op. cit.). The "spike and dome" pattern seems to be more of the nature of "evoked potentials" rather than true epileptic activation of the cortex. More recently with Hunter we have been able to induce not only a "petit mal like" seizure but also a generalized major convulsive attack by local thalamic stimulation, through implanted electrodes in unanaesthetized animals. However it must be made clear that this thalamo-cortical system is not necessary for the maintenance of epileptic activity. The cortex can be undercut without thalamic connections and still maintain a strong after-discharge to electrical stimulation. Also, local after-discharge may be recorded from specific nuclei of the thalamus, after their cortical area of projection has been removed. Consequently each centre is capable of maintaining an epileptic discharge but when they are connected they may influence each other and a reverberating system may be set up.

RELATIONS BETWEEN FORM OF ELECTRICAL ACTIVITY AND PATTERN OF CLINICAL SEIZURES

It is common practice to typify different "kinds" of epilepsy, petit mal, psychomotor, grand mal, etc. according to the form of the associated electrical discharge. We believe that the epileptic process is fundamentally the same in all types of seizure. The myriad forms of seizure reveal the functional characteristics of the area of onset and the neuronal circuits occupied in its path of spread or projection. Even the spike and slow wave complex, especially when confined to a local cortical area, may have no direct relationship to what might be considered clinically as petit mal epilepsy. Certainly the rhythmic sharp waves or six per second waves, more frequently than not, bear no relationship to anything that might be called a psychomotor seizure. Only when their localization of onset is considered, do these patterns have any special significance.

There is one general relationship of form of clinical seizure to pattern of E E G disturbance which must be considered. Seizures whose onsets are marked by generalized "inhibitory" states ("staring", "absence", a retardation or loss of responsiveness or loss of muscle tone, even possibly the generalized paralysis of rational behaviour and memory which characterizes the epileptic automatism ("psychomotor attack") all seem to have a prominent slow wave component in the electroencephalogram recorded from the convexity of the hemispheres. In some of these cases, there may be even a depression in voltage of background activity without slow waves as was pointed out by Dr. Daly at the last meeting of the American Electroencephalographic Society. This suggests the possibility of epileptic activation of special inhibitory mechanisms within the brain but adequate proof of this hypothesis is lacking. We do know that functional paralysis occurs when the integrative function of cortical areas, such as those subserving motor speech

is blotted out by a massive local epileptic discharge This may also be the mechanism of the more generalized inhibitory states' when the epileptic discharge arrests the integrative functions of diencephalic centers concerned with consciousness and the control of behaviour

SUMMARY

1 The only form of electrical activity which is thought to characterize a local epileptogenic lesion of the cortex is the random spike discharge

2 The local spike discharge must become repetitive at a fairly rapid frequency before sufficient activation occurs to cause a change in behaviour or awareness of the patient

3 The spread of epileptic activation is manifest by an enhancement of the background spontaneous rhythms before the form of its activity is changed to a multiple spike pattern indicating violent local autonomous activation of this distant cortical area Specific regions may produce a depression in background activity at the onset of an attack

4 Large areas of the cortex may be activated by electrical signs of epileptic activity with little obvious change in the patient these areas being the anterior frontal region and large portions of the temporal and parietal lobes Spread to subcortical structures seems likely when changes in level of consciousness and behaviour automatisms are associated with epileptic discharge

5 The cerebral cortex alone isolated from connections to subcortical structures is capable of maintaining epileptic after-discharge so that long reverberating circuits are not required for this process

6 Rhythmic epileptic activity of large areas of the cortex synchronized in one hemisphere or bilaterally synchronous from homologous regions of the two hemispheres most probably has its pacemaker in the thalamus since from the thalamus such rhythmic bilateral disturbances can be induced by local electrical stimulation Other subcortical projection systems may also be involved

7 Local cortical epileptic discharge may also be initiated by local thalamic stimulation of the more directly projecting thalamic nuclei

8 Subcortical rhythmic systems projecting to large areas of both hemispheres can also be actuated by local cortical epileptic discharge most readily in certain portions of frontal and temporal regions

9 The clinical pattern of an epileptic seizure is not closely related to the form of associated E E G disturbance but rather to the functional area of the brain primarily involved and the functional characteristics of the neuronal circuits involved in the path of spread

REFERENCES

Dusser de Barenne J G and McCulloch W S Physiological Delimitation of Neurones in the Central Nervous System *Am J Physiol* **1939** *127* 620 628

Adrian E D The Spread of Activity in the Cerebral Cortex *J Physiol* **1936** *88* 127-161

Adrian E D and Moruzzi G Impulses in the Pyramidal Tract *J Physiol* **1939** *97* 153-199

Walker A E Marshall C and Beresford E N Electrocorticographic Characteristics of the Cerebrum in Post-traumatic Epilepsy *Res Publ Ass nerv ment Dis* **1947** *26* 502-515

Pope A Morris Arthur A, Jasper H Elliot K A C and Penfield Wilder Histochemical and Action Potential Studies on Epileptogenic Areas of Cerebral Cortex in the Man and the Monkey *Res Publ Ass nerv ment Dis* **1947** *26* 218-233

Lennox M A and Brodie B Paroxysmal Slow Waves in the Electroencephalograms of Patients with Epilepsy and with Subcortical Lesions *J Nerv & Ment Dis* **1946** *104* 237-248

Jasper H and Droogleever-Fortuyn J Experimental Studies on the Functional Anatomy of Petit Mal Epilepsy *Res Publ Ass nerv ment Dis* **1947** *26* 272-298

Penfield W and Jasper H Highest Level Seizures *Res Publ Ass nerv ment Dis* **1947** *26* 252-271

Dr Gerard

These important findings exemplify yet again the truism that for understanding the nervous system and cerebrum in particular we laboratory scientists must depend heavily and gratefully on our clinical colleagues for problems as well as for their analysis This presentation also leads naturally to an analysis from the physiological side to follow The subject of Mechanisms for the Spread of Epileptic Activation of the Brain" will be presented by Warren McCulloch and discussed by Chester Darrow

MECHANISMS FOR THE SPREAD OF EPILEPTIC ACTIVATION OF THE BRAIN

Warren McCULLOCH, M D
Department of Psychiatry, College of Medicine
University of Illinois, Chicago

In part I was too rushed and in part I was hesitant to write out beforehand what I was going to say because when I knew that I was to follow Penfield and Jasper I knew that some aspect of what I wanted to cover would necessarily have been mentioned I had expected in fact to have heard even more of what I might have written You have already heard from them a description and the beginning of an analysis The habit of breaking down problems of change on the spot into problems of change from spot to spot has always been my way of approaching what goes on when there is a grossly or evidently chemical change

My questions concerning the spread of epileptic seizures can I think be understood better if one does not limit his scope to the treatment of the epileptic seizure but is ready to countenance the spread of the disappearance of activity or the shift to waves of very low rate I would like therefore to outline these pathways of spread and then to go after the seizure itself and after that to contrast it with two spreading states of inactivity

You heard yesterday from Dr Dow about the peculiar restriction of the spread of the electrical sign when you stimulate a folium of the cerebellum It spreads only in the transverse direction of the animal (that is the long way in the folium) and that unquestionably has its anatomical correlate in the beautifully parallel system of fine fibers Now the cerebral cortex contains what has been called a feltwork of fibers As a matter of fact, for the first and important type of spread in the vicinity the feltwork is all-important It has been called a feltwork because the fibers run in all directions and it is in this case easiest to forget the cells that occupy a relatively small fraction of the total volume of the cortex and think principally of the feltwork as fibers crossing in all directions in a space of the order of a millimeter or two millimeters in thickness

Think of a sheet of such material In that feltwork if an electrical stimulus be applied anywhere it is transmitted as what we believe to be action-potentials along these fine fibers at rates that will vary according to anesthesia from about ten to about thirty mm per second The continuity of the cortex always insures that this type of spread is available to any discharge that is set up In the simplest case if one gives a very weak electrical stimulus to the cortex under a light dial anesthesia he finds such a wave spreading out for a distance of about one-half centimeter and dying as it goes Its rate of propagation apparently does not fall off much but its amplitude does and in a short distance it is gone For contrast if one puts his animal under chloralose anesthesia this wave is found to have greater spread This is the *surface-negative wave* This surface negative wave is then found to spread at a higher velocity initially and to fall off both in amplitude and velocity as it travels over the surface of the cortex

I have seen Dr Rosenblueth s experiments on this score and have repeated a few of them and am thoroughly convinced that he is right It depends on the continuity of the feltwork of the cortex It does not jump where there is a sulcus from one side of the sulcus to the other It disappears within and if it comes out at all comes out far later This wave then is travelling distances which are in excess of the distances run by the fine fibers that constitute the feltwork of the cortex Hence one must look to some sort of transmission from one fiber to adjacent fibers or perhaps to cells

and so to their fibers Under these circumstances considerations of the statistical probabilities of connections come into play and one can see immediately that the velocity of the propagation of the wave is a function of threshold for the propagation depends upon getting enough impulses impingent on the next area to increase its activity above the mean threshold of the fibers there If that be the case then an explanation is at hand for something which is at first rather puzzling

If one strychninizes lightly an area say, one-half centimeter in diameter — in the vicinity of the part he is going to stimulate electrically, and then stimulates that point the waves no longer spread as concentric circles like the ripples in a pond but when they come to the strychninized area they seem to leap across it, appearing too early on the far side The one thing which I think we can say about the action of strychnine is that it works wherever synapses are present on cells and there causes them to bunch their firing It does not work on the dorsal ganglion, and it does not work on white matter Hence I think we will have again the same conclusion, that this surface-negative wave spreading from the focus of excitation, if it spreads to any great distance moves transneuronally or from fiber to fiber in the gray of the cortex itself So much for this first type of transmission

Now let us put an animal under deep dial narcosis and stimulate lightly and get only the surface-negative wave We find nothing at a distance As we increase the strength of stimulus there appears at the place stimulated what Adrian called the *surface-positive wave*, and it is now transmitted, not to any great extent in the gray matter itself but goes down into the white fibers that leave this area of cortex to turn up wherever they turn back into the cerebral cortex That it is not dependent on transmission through the feltwork of the cortex is easily assured by simply taking a piece of pipe and heating it up and coagulating a ring around the focus This completely cuts out the spread of the surface-negative wave and has nothing to do whatsoever with the distribution of the remote effects which come over the white matter This is the surface-positive wave By applying strychnine instead of electrical stimulation we have been able to map a tremendous number of these connections from an area to other areas The method depends for disclosing the termini of the axons arising in the strychninized area on there being a sufficiently well-bunched output arriving in the given area There might be fibers arriving in a given area, but if they were not sufficiently numerous or if the velocities of conduction were to differ too greatly one would miss the effect Hence these maps which we have been able to prepare by local application of strychnine in recording of the potential where it arrives gives us a clue as to the general distribution of the spread of seizures in the cerebral cortex

Let me make that clear by one simple example There arise in area 6 enormous numbers of such fibers that go to all of the motor and sensory cortex pre- and post-central cortex extending back to what Brodman called areas 5 and 7 in man and into what he called 39 and 40 in man When the strychnine lies in area 6 all of these areas both of the leg and arm subdivisions show the characteristic strychnine spikes So also do they in the opposite hemisphere and so does area 6 in the opposite hemisphere In other words this is a powerful system of fibers which, if they be activated carry a seizure into all of the first somatic cortex of arm and leg on both sides This is in fact what one finds if one stirs up a so-called *after-discharge* in a lightly narcotized animal (I should say under light dial narcosis) the seizure spreads easily and rapidly to the opposite hemisphere and to the whole of the hemisphere on the same side For contrast area 4 sends no fibers to area 6 and except for a small region in the representation" of trunk sends practically none from either its arm or leg subdivision across to its fellow on the opposite hemisphere If in this same beast one stimulates area 4 instead of area 6 and there produces this after-discharge this motor after-discharge will

spread to that limb and that limb only if the anesthesia be moderate It may spread to the adjacent limb, that is leg to arm or arm to leg, and even from arm to face on the same side, but rarely crosses the midline unless the anaesthesia is so light or the reaction so profound that it starts spreading all over the hemisphere on its own side Then it does cross In other words there is a marked difference in the spread, and the spread corresponds to the known physiologically demonstrated, connections of cortical area to cortical area through fibers in the white matter Notice please, that this is in an animal under dial If that animal is under chloralose the spread in the feltwork of the cortex enables the disorder to pass from area 4 forward into area 6 and one is very often confronted with a grand mal' all over the animal in short order

Now perhaps the most beautiful demonstration of the importance of this second method of spread of seizure is that of Dr Erickson, who I believe, while he was with Dr Penfield made sundry cuts in the white matter and proceeded to show that he could force the seizure in a thoroughly excited cortex to follow the residual paths through the white matter I repeated his experiments on a single hemisphere not on both, after scooping out thalamus and some of the basal ganglia and was able to find the same pathways of spread that he had found and therefore am confident that he was right — and that the spread does not depend on thalamic reverberation And finally I undercut the cortex — the lesion lying deep in the white matter — undercut it completely and had the same picture of spread For this reason I am convinced that the white matter in the region immediately subjacent to the cortex is the chief route of spread of seizures I have laughingly said that so far as I can see it is the only demonstrable function of the corpus callosum to spread seizures from one side to the other I still do not know of anything else we can attribute to it safely

Now there is a third method of spread of seizures which we cannot ignore It is probably more common than we expect and of late has begun to come to the fore There are seizures produced by sundry drugs (I have had the pleasure of working with several of them) which cause seizures which may start in the cortex or in other structures, but in which the seizures in the cortex play jack-in-the-box You have them now at one place and then they disappear out of the cortex and then they reappear somewhere else in the cortex After awhile we became suspicious and began placing electrodes in the depths The jack-in-the-box seizure is not a series of seizures starting independently in the cortex If one has enough electrodes in the lower structures one sees it is a seizure which disappears out of the cortex but persists in some lower structures and then from them reappears in the cortex I would like to mention here one that is probably well known to you and that is the type of convulsion produced by DDT The material undoubtedly makes its greatest inroad on the nucleus dentatus of the cerebellum In records from the surface of the brain the seizure appears in the cerebellar leaves first and only after the cerebellar seizure has been underway for awhile does the seizure normally appear in the cerebellum where it pokes up into areas 4 and 6 This is exactly what one would expect if the seizure were transmitted up the superior cerebellar peduncle and relayed to the cortex

There are a series of drugs which like DDT produce seizures that appear first in the cerebellum They may not begin in the cerebellum They may begin somewhere in the deeper structures and pop up into the cortex of the cerebellum The pathway from there to the cerebral cortex is certainly wide open for seizures When one maps the deep structures in which one picks up these seizures that were in the cerebral cortex disappeared and reappeared in it they have quite proper paths including the thalamus and the midbrain Now their jack-in-the-box ways are not necessarily due to the drug Dr Kopeloff was kind enough to let Dr Ward and me have one of his monkeys and the monkey was kind enough to go into status when we opened him up We saw the typical spread

of seizures following principally the path laid down in the subjacent white matter, and then we encountered the jack-in-the-box seizures The seizure in the cortex would disappear from all of our cortical electrodes, we could find no trace of it and then would come bobbing up again We had electrodes in the thalamus hypothalamus, etc It became fairly clear that in almost all of the cases in which the seizures disappeared out of the cortex they were persisting in lower structures, and they did reappear in the cortex in proper relation to the particular lower structures I should say that our hypothalamic electrode, while it did show seizures in some cases, never showed any that bore any relation to the cortical seizure So this third method of spread is unquestionably to be kept in mind It is a spread out of the cortex into some other structure and then a return to the cortex

Now, as for the signs of spread Perhaps fortunately, perhaps unfortunately, I began work on cortex with a direct-couple amplifier With a direct-couple amplifier when you place strychnine anywhere on the cortex, you see that area which is strychninized become for a period of several minutes increasingly and then remain electrically negative — a matter of 50 millivolts — to remote regions of the cortex As it becomes negative, small negative spikes appear on its rising negativity They are and I say it unhesitatingly, a discharge of the superficial layers of the cortex One has only to thermocoagulate the superficial layers at that minute, and they are gone As the strychnine soaks into the depths the deeper layers of the cortex begin to fire before the superficial layers and one obtains an initial positivity of the surface followed by a negativity and that, in turn followed by a positivity One is now dealing with a seizure a spike which is beginning in the depths of the cortex arising to the surface spreading to a wider area, and then descending again By undercutting, or thermocoagulating immediately under the area where one has applied his strychnine one prevents transmission to remote portions from the initial surface positivity but not from the second surface positivity, that is, the first discharge in the depths is limited to the area under which the lesion interrupted the fibers The second after the spread to a wider area as a surface negative wave descends from the cortex not undercut We have then from this simple experiment the significance of the sign of the potential I should say we can confirm this easily by thermocoagulating the superficial layers of the cortex, say the outer two or three layers at the time when the strychnine spikes have their initial positivity, for that initial positivity is enhanced and there is no negativity and no second positivity under those circumstances There are only the deeper layers to fire, and only the strychninized cells firing Now this gives us an interpretation of the signs and potentials which is entirely in harmony with everything that is known about ascending disturbances which we may initiate by stimulation of the body, or the thalamus, or anywhere up the sensory stream When the disturbance is coming up into a heavily narcotized cortex, let us say under dial the only sign that one gets is a surface positivity restricted to the area where the incoming fibers terminate If the cortex be somewhat less narcotized this is followed by a negativity if it be still more lightly narcotized, by a second positivity In other words the disturbance ascending turning over and going down again gives us the sequence Positivity, negativity positivity What has this to do with the spread of the seizure? The disturbance, is, so to speak, negative where it happens, positive at a distance

In Dr Jasper's records you saw the spike starting negative where it happened on the cortex, followed with a much larger positive wave This is I would say the most accurate way one could define a disturbance — as something starting in the superficial layers of the cortex and spreading to the depths And you will notice that then at a remote region, into which this spike is propagated, it appears first as a little bit of a positive spike followed by a large negative wave If you start a seizure in area 6 and record from area 4, while the seizure is buzzing

away in area 6 you will find a positive wave in area 4 This is under deep dial so that the fit will not spread hence you find the positivity in area 4 corresponding to the negativity in area 6 perfectly timed The rate of that spread, the rate of travel of that potential must be at least and may be a good deal more than 50 meters per second So in the interpretation of any record one expects that if he has a focus in point A discharging and from that focus impulses are being poured into cortex at point B he will have a positivity at the recipient corresponding to the negativity at the starting point The outgoing potential wave from the cortex as the initial negative and then positive sequence will be reflected in a positive wave with a big negative wave after it at the recipient area Now curiously enough when you do stir up an after-discharge the area which is discharging shown by direct-couple amplifier is negative to remote regions And a recipient area builds up its negativity only when it begins to go off itself, that is when it begins to show sharp negative bursts of any zone I am speaking now of a direct-couple amplifier pick-up You lose this with the longest time capacity coupled amplifiers that I have at my disposal It is a slow growth of voltage over many minutes

One more point I should like to mention There are two other electrical changes which spread in the cortex One of those I will call suppression, and the other the spreading depression If one stimulates area 4S in man or animal (and for the figures on man I am indebted to Dr Wyke) one starts up a process which goes through the nucleus caudatus and thalamus I do not know the course from nucleus caudatus to thalamus even now although I have puzzled over it for years This process blocks activity in the thalamus The electrical activity of the cortex after a latency that depends on the depth of anesthesia disappears for a time that depends on the depth of anesthesia and on the distance from the focus My figures were all obtained from animals under dial narcosis Dr Wyke s figures were obtained on the human cortex without narcosis and therefore are far more important I have his permission to mention them today The rate of spread of electrical inactivity from area 4 over the cortex is about 1 5 centimeters per second and that is only plus or minus a small figure about 0 2 The latency is some 5 seconds and the duration of inactivity at any place is some 55 seconds Without narcosis this thing can be repeated again and again Now what is characteristic about this on the cortex is that even with direct-couple amplifiers during the period of inactivity of the cortex there are no slow oscillations

Let me contrast this now with spreading depression As opposed to this slow inactivity which spreads all over the cortex there is another slow inactivity which one can elicit by stroking cortex almost anywhere It is in the first place accompanied by vascular changes which spread with the inactivity over the cortex The vascular change is visible In the second place depression spreads at about one-third of a centimeter per second Now there is a crucial difference between these two with respect to many things And I want to liken them in their own ways to the inactivity at the end of a seizure In the post-convulsive silent period in your electrical records you are dealing with a silence which is due to exhaustion of elements that have been acting I will call this for the sake of simplicity exhaustion or extinction It always means that those cells that have been active are tired As opposed to this in the case of suppression of electrical activity there is on stimulation of area 4S during the electrical inactivity of the cortex an associated inability to evoke responses by stimulation of area 4 although the patient is at the time able to move voluntarily again from Dr Wyke s observations on man Now during the spreading depression there is no such inability to elicit responses from area 4 or change in the ability to move a Parkinsonian arm There is only electrical inactivity recorded from the cortex and during the spreading depression there is a slow oscillation of voltage too slow to be recorded with any of our ordinary capacity coupled instruments but of large magnitude and per-

sistent Finally there is a marked difference between the return of activity in all of these cases You are perfectly familiar with the return of activity after a seizure The return of activity after stimulation of area 4S appears in the animal under narcosis as a series of spindles that are very characteristic Dr Wyke informs me that in man without narcosis you get only one spindle of 5 to 6 c p s activity and then abrupt return to the normal level of activity The spreading depression shows a slow return toward the normal frequency — quite another return

This brings me to the final point The spreading depression has the peculiar property that Ralph Gerard s famous caffeine spike has — you can section the cortex and butt the parts together and it crosses the cut Whatever this mechanism is it depends probably on electrical and chemical continuity not on anatomical structure running from one area to the other I do not know what role this may play in the spread of seizures and I think for the moment all I can say is until such time as we have studied what kind of discharge we can get to go on out of an area that has been entirely surrounded by cuts, I would be loath to deny that it might be of importance

MECHANISMS FOR THE SPREAD OF EPILEPTIC ACTIVITY OF THE BRAIN

Chester W Darrow

Institute for Juvenile Research, Chicago

In an attempt to formulate in advance Dr McCulloch's probable approach to the problem of the spread of epileptic discharge the one thing I correctly anticipated was that I should be able to contribute very little in addition to his analysis of mechanisms involved For years he and his collaborators have been studying spread of neuronal activity by the strychnine spike technic In his hands the method has become not merely an object of research but a tool for physiologically tracing the neural connections of the brain That spread of discharge may occur by way of subcortical association pathways as well as by spread within the feltwork of the cortex he and his collaborators have amply demonstrated To his clear presentation of the mechanisms presumably involved in the spread of the strictly convulsive discharge I have little to add

I was asked also to elaborate somewhat on the possible role of vascular changes which have frequently been observed to accompany the epileptic discharge You may recall that it was Hughlings Jackson who in 1870 suggested the possible importance of vascular mechanisms when he wrote It is I speculate through the arteries that sequence of movements is developed whether those movements be spasm passing up the arm and down the leg or whether they be the orderly sequences of movements in health " This view may seem naive to today s investigator possessed of modern information regarding the intrinsic response of cerebral blood vessels to pressure to carbon dioxide or to diminished oxygen and concerning the various humoral mediators and autonomic effectors to the cerebral blood vessels But as has so frequently happened Jackson s speculations were not without some subsequently confirmed factual foundation

I am sure I need not more than mention to this group the several studies which have confirmed the tendency for increased blood flow to attend epileptic discharge from the cortex Gibbs Lennox and Gibbs (5) Penfield (10), Penfield von Santha and Cipriani (11) Erickson (3), Kennedy Wortis and Wortis (9), and Finesinger and Cobb (4) are among the earlier observers of this phenomenon Dr Graf and I observed the effect photometrically in one animal in which convulsions occurred following slow activity induced by hyperventilation (1) One s first guess would be that the effect is of the same origin and bears the same relation to the neural activity of convulsions as increased blood flow bears to neuronal activity following stimulation as shown by von Santha and Cipriani (12) and by Serota and Gerard (13) Whether the dilatation is secondary to an increased metabolism with increased CO_2 mediating the dilator response or to some other mediator is at present anybody s guess

These effects of spread and accompanying increased blood flow so far discussed have been those attending tonic-clonic or so-called grand-mal' types of epileptic discharge In many respects these should probably be contrasted with the circulatory and other conditions frequently associated with the three per second spike and wave phenomena commonly designated as petit mal You will recall that Gibbs (6) early called attention to the chemical differences between the two groups grand mal patients tending to have an excess and petit mal patients a deficiency of carbon dioxide in the blood as compared with normal persons The contrast is further emphasized by the ease with which a little hyperventilation will blow off the carbon dioxide and precipitate petit

mal seizure in susceptible persons and the infrequency with which the procedure will precipitate grand mal What is more, hyperventilation should favor cerebral vasoconstriction not the dilatation reported for grand mal The ease with which petit mal seizures may sometimes be terminated by carbon dioxide or by sensory stimulation may also be contrasted with the fact that these are conditions which sometimes precipitate grand mal In keeping with this contrast I would like to suggest certain peculiarities relating to the spread of the petit mal attack which have come to the attention of Dr Charles Henry and me as we have studied the changes when registering activity over an entire hemisphere by means of simultaneous monopolar and bipolar recording technic

As might be inferred from this enumeration of contrasts the conditions favoring spread of slow waves across the cortex may be different from those favoring spread of spike-like sharp effects and grand mal convulsions I wish to point out that the moderate decrease of cortical activity by drowsiness, by certain drugs, by trauma by hypoglycemia and by hyperventilation separately or in combination one with the other may provide a condition in which the intrinsic faster activity of the cortex is reduced and, possibly as a consequence, susceptibility to external electrical neuronal and photic influences is increased It is a condition in which the cellular elements of the cortex, possibly because of absence of preoccupation, are more readily regimented *en masse*, more readily driven from without or from below, and in which they are more profoundly susceptible to the spread of slow activity It is a condition which is combatted in some cases by those pharmacologic agents which in moderation may be able to maintain intrinsic fast cortical activity in frontal and motor areas possibly thereby preventing hypersynchronous slow wave regimentation by an outside or lower level dictator Differences between simultaneously recorded monopolar and bipolar activity often appear consistant with this interpretation Spread and development of slow wave activity over the surface may be also seen

Dr Henry and I have frequently had occasion to note in subjects who develop petit mal spike and wave patterns following hyperventilation that a sustained discharge of three per second hypersynchronous slow waves starting locally, tends to spread across the cortex and precede the appearance of the three per second petit mal spike and wave effect If the slow activity fails to extend into the frontal and temporal regions possibly including some deeper lying structures, no spike may develop Once however, the slow activity has spread to frontal and temporal areas a spike discharge may occur and set off a new slow wave which will then again spread across the cortex trip another spike discharge and start another cycle

What I have tried to suggest is that there may be different mechanisms involved in the spread of different types of epileptic discharge Conditions favoring grand mal convulsions may typically involve lowered thresholds increased ease of cortical excitation, increased metabolic activity and associated increased cerebral circulation High voltage slow and petit mal type discharge on the other hand may be best favored when circulatory, chemical and other conditions limit intrinsic activity among cortical elements and thereby render them more susceptible to internal or external synchronization

REFERENCES

1 Darrow C W and Graf C G Relation of electroencephalogram to photometrically observed vasomotor changes in the brain *J Neurophysiol* 1945 *8* 449-462

2 Darrow C W Green J R Davis E W and Garol H W Parasympathetic regulation of high potential in the electroencephalogram *J Neurophysiol* 1944 *7* 217-226

3 Erickson T C Spread of Epileptic Discharge an experimental study of the after-discharge induced by electrical stimulation of the cerebral cortex *Arch Neurol and Psychiat* 1940 *43* 429-452

4 Finesinger J E and Cobb S Cerebral Circulation Action on the pial arteries of the convulsants

caffein absintne camphor and picrotoxin Arch Neurol and Psychiat 1933 30 980-1002
5 GIBBS F A LENNOX W G and GIBBS E L Cerebral blood flow preceding and accompanying seizures in man Arch Neurol and Psychiat 1934 32 257-272
6 GIBBS F A Electroencephalography in epilepsy J Pediatrics 1939 15 749-762
7 JACKSON J H A study of convulsions In Taylor J Holmes G and Walshe F M R Selected Writings of John Hughlings Jackson London Hodder and Stoughton 1931 1 8 36
8 JASPER H H and ERICKSON T C Cerebral blood flow and pH in excessive cortical discharge induced by metrazol and electrical stimulation J Neurophysiol 1941 4 333-347
9 KENNEDY F WORTIS S B and WORTIS H The clinical evidence for cerebral vasomotor changes Res Publ Ass nerv ment Dis 1938 18 670 681
10 PENFIELD W The circulation of the epileptic brain Res Publ nerv ment Dis 1938 18 604-637
11 PENFIELD W SANTHA K VON and CIPRIANI A Cerebral blood flow during induced epileptiform seizures in animals and man J Neurophysiol 1939 2 257-267
12 SANTHA K VON and CIPRIANI A Focal alterations in subcortical circulation resulting from stimulation of the cerebral cortex Res Publ Ass nerv ment Dis 1938 18 346 362
13 SEROTA H M and GERARD R W Localized thermal changes in cats brain J Neurophysiol 1938 1 115-124

BIOCHEMICAL APPROACHES IN THE STUDY OF EPILEPSY[1]

K A C ELLIOTT
Montreal Neurological Institute

In the following discussion I shall consider only chemical factors possibly concerned in the initiation of epileptic activity in the brain of the epileptic subject I think we have to consider three groups of possibilities

(1) The abnormal physiological and underlying chemical behavior of the nervous tissue in epilepsy may be a normal response of normal neurones reacting to an abnormal environment

(2) The abnormal behavior may be due to changes in the chemical potentialities of the neurones

(3) Changes in the chemical potentialities of the neurones may occur but secondarily to the hyperactivity as an adaptation to abnormal conditions and may not be essential to the epileptic process

We have made a study of the energy metabolism *in vitro* of a considerable number of samples of tissue excised by Dr Penfield from human epileptic patients No sign was found that the respiration rate or effect of calcium on respiration rate was different from what might be expected from normal human brain tissue Values for normal human brain were estimated from a study of brains from a series of animals of different species There was also no sign that the epileptogenic tissue differed from the probable normal in respiratory quotient or in rates of ærobic or anærobic glycolysis Similar results were obtained with brain from a dog rendered epileptic by the 'agenized' diet and from an area of dog brain showing abnormal electrical activity following treatment with alumina cream

We are inclined to believe that the first of the three possibilities mentioned above may be true namely that epileptogenic brain tissue contains normal neurones which are subjected to abnormal stimuli Of course such a thesis rests on slim foundations as long as only energy metabolism studied *in vitro* is considered It is our immediate intention to study aspects of acetylcholine synthesis liberation and destruction in normal and epileptogenic tissue since this type of metabolism is likely to be closely connected with function in nervous tissue A couple of years ago Dr A Pope working in collaboration with a number of us in Montreal obtained evidence that choline esterase activity was higher in brain tissue from epileptogenic foci than in samples of brain from other areas But I think it possible that such an increase in activity may represent a secondary adaptive change and not be primary to the epileptic process Dr Donald Tower working with Dr McEachern in Montreal has found that usually a detectable amount of acetylcholine is to be found in the spinal fluid of epileptic patients and animals This may indicate an increased acetylcholine release in the brain so that some of it finds its way into the subarachnoid space The concentration at least in the spinal fluid is so far below the optimal for choline esterase activity that it would scarcely be affected by the esterase Reliable detection of free acetylcholine in the brain tissue *in situ* is at present a very difficult problem But it is possible that the level of free acetylcholine in the brain tissue is raised in epilepsy towards the threshold concentration for its action so that any new release of acetylcholine as a result of normal processes will set off activity abnormally readily However it seems to me that Dr Tower s finding may simply be the *result* of neuronal hyperactivity and may not indicate the basis for this activity

[1] From the Department of Neurology and Neurosurgery McGill University and the Montreal Neurological Institute Reprint no 290

The fact that such a wide variety of drugs and physiological conditions can produce convulsive seizures in normal animals does indicate, to my mind that there is no need to postulate a change in the chemical potentialities of neurones to account for most epileptic conditions On the contrary I feel that we need more than anything the type of understanding of brain and nerve processes which is developing out of the work of Dr Bronk and his colleagues What types of factors will produce lowered thresholds to stimulation, or hyperactivity, in normal nervous tissue? Dr Bronk's earlier studies on calcium deprivation have given us useful leads in this area What are the conditions with regard to supply and demand of oxygen in living brain and nerve tissue? The work of the Johnson Foundation is helping us rapidly in this regard I feel that correlation of this type of information with *in vitro* studies will soon give us clearer ideas regarding the control of nervous activity

For instance *in vitro* work has taught us that brain tissue is capable of rapid glycolysis acid production especially anaerobically If the blood supply and hence the oxygen tension, in a given local area falls below a certain low level rapid glycolysis would set in Acid would be produced intracellularly It seems likely that a change even temporary in the relation of the intracellular pH to the extracellular pH would have considerable effect on the distribution of inorganic ions and might affect the liberation of acetylcholine and so affect neuronal activity (Quastel and his co-workers found that a fall in pH to 6 0 — 6 5 accelerated the liberation of free acetylcholine from its precursor) The effects on the pH of extracellular fluid may be the basis for the action of the ketogenic diet in controlling some epilepsies and of hyperventilation in provoking seizures

Measurements of cortical pH have given us some necessary information but so far I do not think they have given us specific information regarding epilepsy Dr Jasper and I find that the pH of the surface of the normal cortex varies from nearly equal to that of the venous blood to considerably lower The variability seems to be related to the proximity of large blood vessels a situation similar to that found for oxygen tension by Dr Bronk s group The pH at a given point has been shown by Dusser de Barenne Nims and others and by Jasper and Erickson, to undergo changes during seizures but these changes appear to be the result of rather than primary to the seizure They can be explained on the basis of excessive acid production during hyperactivity and reactive hyperemia which would tend to raise the pH toward the blood level Possibly more closely relevant are the observations of Dusser de Barenne and McCulloch that the pH of the cortex seemed to be increased when the phenomenon of facilitation" was observed and lowered during the period of extinction' A group of us at Montreal found no obvious sign of abnormal pH in focal epileptogenic areas in monkeys and this type of study will need application of more refined methods if significant observations of differences in small local areas are to be understood

The studies of Dr Bronk's group on the role of calcium in controlling nervous activity need to be borne in mind Quastel and his co-workers noted that lack of Ca caused increased liberation of acetylcholine in brain The availability of calcium ion is likely to be affected by pH changes and also by certain intermediary metabolites notably citric acid which could conceivably accumulate when metabolism is interfered with by circulatory or other factors We are giving some attention to this possibility

Changes in oxygen supply and pH are not the only factors in structural and circulatory abnormalities which could affect nervous function One must consider glucose concentration CO_2 tension and the possible accumulation of other metabolic end products Deprivation of glucose the normal substrate of brain respiration naturally affects nervous function and this is seen in insulin stupor and convulsions Feldberg found maximum acetylcholine synthesis or rather release in the presence of a low concentration of glucose lower than that in

normal blood The normal blood concentration was inhibitory and he suggested that certain physiological processes might be controlled by glucose concentration Quastel and his co-workers found a much greater effect of potassium on synthesis and release of acetylcholine by brain tissue *in vitro* in the presence of bicarbonate-CO_2 buffer than without this buffer but they did not elaborate on a physiological significance of this effect of CO_2 or bicarbonate Keto acids like pyruvic acid have been found by Nachmanssohn and others to inhibit acetylcholine synthesis the concentration of these might be affected by blood supply

The possibility that an abnormal amount of some blood constituent may be found and provide a clue to the epileptic mechanism has been considered by many workers but I do not believe that any real answer has come from such studies Some years ago Murray and Hoffmann reported high basal values for substances estimated as guanidine in the blood of essential epileptics and found the value greatly increased at the time of seizures This seemed specially interesting since guanidine is itself a convulsant and it is structurally related to a number of compounds essential in normal metabolism Unfortunately we have not been able to confirm this finding in any type of epileptic

I feel that the studies of Dr Penfield and his colleagues indicating a probable impairment of local circulatory control in the neighborhood of epileptogenic foci is as likely a starting point for chemical theories and experimentation as any we have at present

I have considered only factors concerned in clinical epilepsy There are numerous chemical agents which can produce convulsive effects or epileptiform brain waves but in most cases we have scarcely any idea of the mechanisms of their actions Acetylcholine and the choline esterase inhibitors perhaps cause an exaggeration of normal processes Citrate immobilizes calcium ion Fluoroacetate is known to interfere with acetic acid oxidation in tissues other than brain But since in the brains of species most studied acetic acid is not normally oxidized anyway the chemical action of fluoroacetate as a convulsant is not clear I feel that more knowledge of the locus of chemical action of drugs like metrazol and of the biochemical basis of action of anticonvulsants is one of the most essential requirements for the understanding of the chemistry of epilepsy

THE NEUROPHARMACOLOGY OF ANTIEPILEPTICS [1]

James E P Toman, Ph D

Department of Physiology, University of Utah College of Medicine, Salt Lake City

INTRODUCTION

Research in the therapy of convulsive disorders has advanced at a remarkable pace during the past decade The acceleration in this field is well illustrated in table I Since recent progress has depended to a large extent upon the development of quantitative experimental methods for the evaluation of new drugs the present survey will be devoted primarily to a discussion of experimental findings which suggest possible mechanisms of action of antiepileptic agents

I MECHANISM OF CONVULSIVE SEIZURES

A knowledge of the mechanism of antiepileptic action presupposes an equal knowledge of the physiology of seizures In a previous review (97) this subject has been developed at some length Only the briefest summary will be given here

The primary lesion giving rise to seizures may be of vascular or other origin but Jackson's 'occasional, sudden excessive rapid, and local discharges of grey matter' (49) must arise from neurones The discharges may originate in cells made transiently hyperexcitable by ischemia (73) or in some instances may arise in otherwise normal areas which have lost their intrinsic inhibitory system of neurones through previous injury (97) Adrian and Moruzzi (1) have recorded action potentials from single pyramidal fibers of the cat after excessive chemical or electrical stimulation of the motor cortex, or during seizures initiated from other cortical regions The characteristic activity consisted of bursts of impulses of unusually high frequency 1000 per second or more These discharges appear to represent the maximal degree of activity of central neurones an excessive responsiveness evoked by excessive stimulation Moruzzi (72) believes that these high-frequency bursts constitute the mechanism by which convulsive activity spreads progressively throughout the brain The successive involvement of normal areas in a seizure may also be aided by the breakdown of inhibitory mechanisms under excessive stimulation as postulated by Bubnoff and Heidenhain (9) There may even be a transformation of inhibition into excitation as suggested by Sherrington (86) Such a possibility is compatible with the recent Brooks-Eccles (8) hypothesis of inhibition by subliminally-activated short neurones Whatever the mechanism of initiation and spread the ultimate manifestation of excessive cerebral stimulation in all mammalian species is a tonic-clonic seizure of stereotyped pattern and simple properties (100)

The number and variety of clinical seizure manifestations may be formally explained on the basis of four factors

(a) *The focus of origin of seizure discharges* One of Jackson's (49) great contributions was the correlation of various sensory aura and limited motor seizures with anatomical lesions The same concept has now been extended to various types of psychical seizures with the demonstration by Gibbs and Gibbs (27) and Penfield and Jasper (74) of frontal and temporal foci in psychomotor epilepsy and the presentation of evidence by Jasper and Drooglever-Fortuyn (50) for a midline diencephalic origin of petit mal dysrhythmia

(b) *The extent of spread from the focus* The anatomical pathways for spread of convulsive activity and the correlation

[1] Original investigations reported in this communication were supported by grants in-aid of research from the Division of Research Grants and Fellowships of the National Institute of Health U S Public Health Service

Table I — Some useful antiepileptic drugs

Antiepileptic	*Introduced by*	*Major usefulness in*	*Selected references to Literature*
Bromide	Locock 1857 (62)	Grand mal	2 53 62 67 94 99 100 104
5-phenyl-5-ethyl barbituric acid (Phenobarbital Luminal)	Hauptmann 1912 (45)	Grand mal	18 40 41 45 48 51, 52 54 63 67 85 90 99 100
3-methyl-5-phenyl-5-ethyl barbituric acid (Mebaral Prominal)	Heyde 1932 (47) and Blum 1932 (7)	Grand mal	7 13 38 47 70 84 99, 103
5-5-diphenyl-hydantoin (Diphenylhydantoin Dilantin)	Putnam and Merritt 1937 (78)	Grand mal Psychomotor	3 4 5 10 11, 17 22 24 25, 26, 28 30 31 32 35 40 42 43 44 46 53 55 58 66 67, 68 71 76 78, 80 93, 94 96, 99, 100 102 105
3 5 5-trimethyl-oxazolidine-2 4-dione (Trimethadione Tridione)	Richards and Perlstein 1945 (82)	Petit mal	6 14 15 16 22 34, 37 40 57, 60 75 81 82, 87 88 95 99 100
3 methyl-5-phenyl-5-ethyl-hydantoin (Mesantoin)	Loscalzo 1945 (64)	Grand mal Psychomotor	12 56 59 64 65, 92, 94 99
5-diphenylene hydantoin (Diphenylene diimide)	Fabing et al 1947 (23) Merritt and Brenner 1947 (66)	Grand mal Psychomotor	23 55, 66
3 5-dimethyl-5-ethyl oxazolidine-2 4-dione (Paradione)	Davis and Lennox, 1947 (15)	Petit mal	15, 21 89
5 5-diphenyl oxazolidine-2 4-dione (Epidon)	Ellerman 1947 (19 20)	Grand mal	19 20 69 77
5-phenyl-5-thienyl hydantoin	Peterman 1948 (76)	Grand mal	36 76
Phenacetylurea (Phenurone)	Gibbs Everett and Richards 1948 (29)	Grand mal Petit mal Psychomotor	21a 29 89

of motor signs with extent of spread have been studied in experimental animals particularly by Rosenblueth and Cannon (83)

(c) *The intensity and distribution of activity arising from the involved centers* The various gradations of seizure discharge have also been studied (83) The grouping of spike discharges during clonic activity is a typical example.

(d) *The aberration of function resulting from secondary hypersynchronization of non-convulsing centers* This factor may play an important role in the arrest of consciousness during petit mal attacks (50)

II MECHANISMS OF ANTICONVULSANT ACTION

Assuming that the ultimate manifestations of a clinical seizure depend upon the occurrence of a series of processes anticonvulsants may conceivably exert their characteristic actions by blocking any one or more of these processes and the points of blockade may differ from one agent to another It is the purpose of this section to consider some of the possible modes of action of anticonvulsants

A Upon non-neural lesions

Although vascular lesions may be of etiological importance in the formation of epileptogenic foci (73) the reported effects of a number of autonomic drugs upon experimental seizures have been minor (94)

B Upon neurones

Since seizures represent the aberrant behavior of neurones it seems justifiable to inquire concerning the effects of anticonvulsant drugs upon properties of neurones The following observations upon frog sciatic nerve (98) show the potential value of such an approach

(a) Frog sciatic nerve when stimulated with brief shocks of intensity sufficient to cause a subsequent overshoot of membrane voltage responds with a double action potential spike (Fig 1) The second or rebound spike occurs 3 to 6 msec after the ordinary initial compound spike and represents the synchronized firing of a large fraction of the myelinated fibers of fast conduction The phenomenon is dependent on rapid accommodation causing a high degree of supernormality in the recovery period following the response to a supramaximal shock Both the ultrasupernormality' and the consequent rebound spike are abolished by diphenylhydantoin in concentration as low as 0 05 mM/1 approaching the calculated therapeutic blood level in man Phenobarbital Epidon Nirvanol and Phenurone are effective in concentrations of 1 mM/1 or less

(b) When stimulated with a brief series of supramaximal repetitive shocks the nerve undergoes an abrupt decrease in threshold to about half the normal value and thereafter recovers slowly over a period of several minutes Phenobarbital in particular and a number of other anticonvulsants are capable of preventing this prolonged hyperexcitability induced by excessive stimulation

(c) Frog sciatic nerve, after immersion for an hour or more in neutral isotonic sodium phosphate solution undergoes a reduction in threshold to the point of spontaneous firing Single supraliminal shocks are followed by repetitive synchronized discharges (Fig 1) These effects are abolished by various anticonvulsants in approximately the same concentrations which prevent rebound spikes following supramaximal stimulation in Ringer s solution Another effect of phosphate treatment is to increase the permeability of nerve to sodium ion as indicated by an increased rate of exchange and higher equilibrium value of radioactive sodium Diphenylhydantoin prevents this effect Other anticonvulsants have not yet been tried

The repetitive behavior produced by excessive stimulation or by lowering of threshold of frog sciatic nerve resembles in many ways the repetitive character of the seizure discharges studied in pyramidal neurones by

Adrian and Moruzzi (1) It is somewhat premature to relate these peripheral nerve findings to the convulsive activity of brain cells, but the parallelisms are striking

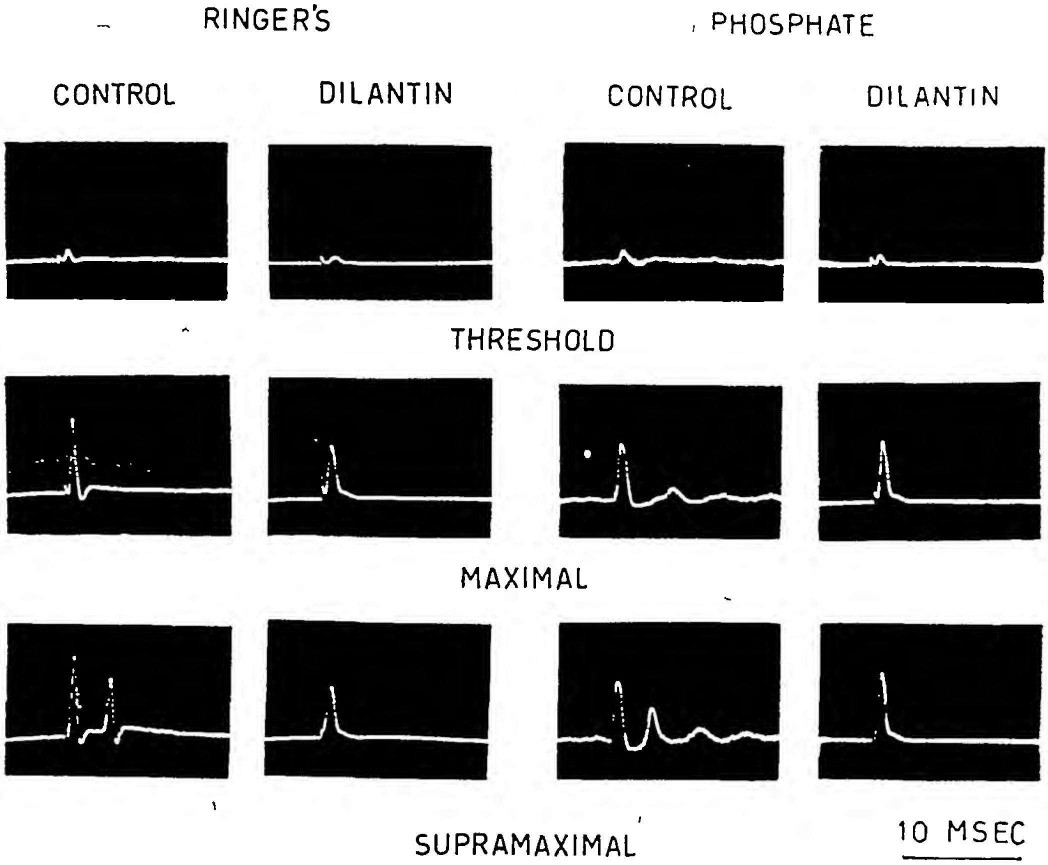


Fig 1 — Effect of diphenylhydantoin (Dilantin) on excessive responsiveness of frog sciatic nerve

Action potentials of sciatic nerves of R *pipiens* recorded in moist air at 30°C Initial deflection indicates shock artifact of 0 1 msec rectangular stimulating pulse Conduction distance 15 mm The four vertical columns show typical responses of four individual nerves treated as follows (all solutions adjusted to pH 7 35)

First column Control nerve after five hours in frog Ringer s solution Upper record response to just supraliminal shock Middle, response of all alpha fibers to just maximal shock Lower double response to a shock of 15x threshold intensity the second or rebound spike represents the hypersynchronized discharge of most of the previously responding alpha fibers

Second column Paired nerve after five hours in Ringer s solution containing diphenylhydantoin sodium 5 x 10^{-5} M Lower tracing shows absence of rebound spike

Third column Phosphate control nerve after two hours in isotonic mixture of mono- and disodium phosphate solutions Upper tracing shows random repetitive firing and threshold response to shock which was approximately 50% of control value Middle and lower records show oscillating hypersynchronized responses with maximal and supramaximal shocks

Fourth column Paired nerve after two hours in phosphate solution containing diphenylhydantoin sodium 5 x 10^{-5} M showing absence of phosphate effects or rebound spike

as membrane potential, threshold, spike amplitude and duration conduction velocity and recovery process, when these are studied with submaximal stimuli in frog Ringer s solution

The more useful anticonvulsants have been found to have relatively minor effects on such ordinary properties of frog sciatic nerve

lution It is possible that these and other properties may be more dramatically altered in the more sensitive cerebral neurones, parti-

cularly when the latter are made hyperexcitable by injury ischemia or other circumstances conducive to the formation of epileptogenic lesions

C Upon non-convulsive behavior of the central nervous system

The more effective antiepileptic agents are noteworthy for their ability to suppress spontaneous seizures in man and to modify or prevent experimental seizures in animals in doses which produce no overt changes in ordinary behavior Nevertheless it is relevant to examine more closely the effects of anticonvulsants upon the excitation and response characteristics of the non-convulsing brain in the hope of recognizing quantitative changes which become crucial for the initiation and spread of a seizure An attempt in this direction has been made by studying nonconvulsive EEG and motor responses of unanesthetized rabbits to electrical stimulation or to sub-convulsive doses of metrazol Some of the results may be briefly summarized

(*a*) *Electrical threshold* Some agents including phenobarbital and Trimethadone produce a moderate increase in electrical threshold for motor and EEG responses (40) Trimethadione is particularly effective in preventing the lowering of threshold produced by metrazol Diphenylhydantoin has relatively little effect upon threshold for single isolated shocks However a demonstrable increase in threshold for movement elicited by repetitive shocks can be seen when the frequency is considerably above or below the optimum region of the frequency-response curve (98)

(*b*) *Recovery of excitability* Following an adequate cortical stimulus there occurs a relatively supernormal phase with a peak at from 2 to 4 msec and a relative subnormal excitability up to approximately 200 msec Diphenylhydantoin has no consistent effect on this process Phenobarbital tends to prolong the subnormality but the effect is marked only with sedative doses and is seen with other barbiturates such as pentobarbital which are not remarkable for their anticonvulsant action (98).

(*c*) *Spontaneous EEG changes* The effective anticonvulsant drugs have relatively little effect on the resting EEG in doses which are adequate to modify seizures but less than sufficient to produce overt neurological signs such as sedation ataxia etc Trimethadione phenobarbital and other sedative drugs cause the appearance of sleep-like activity (fast spindles and irregular slow waves) in doses producing drowsiness (40).

(*d*) *Evoked EEG responses* The complex responses evoked by cortical stimulation are changed by sedative doses of Trimethadione and barbiturates to spindle activity of the type seen in the spontaneously drowsing animal (40)

(*e*) *Metrazol EEG responses* Subconvulsive doses of metrazol produce a typical pattern of recurrent high voltage regular 5/second slow wave episodes which also characterize the response to electrical stimulation Diphenylhydantoin is without effect upon these discharges but phenobarbital and Trimethadione increase the dosage of metrazol required for their appearance Trimethadione is highly effective in restoring the metrazol-altered EEG toward normal (40)

D Upon experimental seizures

(See also section III)

The clinically effective antiepileptic drugs show one or more of our distinct actions upon experimental seizures

(*a*) *Increase in electroshock seizure threshold* Trimethadione and phenobarbital are representative of the group of anticonvulsants having moderate ability to raise seizure threshold In this respect they are far exceeded by Phenurone Diphenylhydantoin has questionable action upon seizure threshold at least when brief electroshock stimulation is used and the least detectable seizure is taken as endpoint (96)

(*b*) *Prevention of abnormal lowering of threshold* All of the clinically effective antiepileptics yet tested possess in some degree the ability to prevent the lowering of electroshock seizure threshold which can be produced in rats by oral hydration or by extracellular electrolyte depletion (93).

(*c*) *Increase in threshold for metrazol-induced seizure* There is a rough correlation among anticonvulsants between ability to raise electroshock seizure threshold and ability to increase the dosage of metrazol required for induction of seizures but the differences are sufficient to suggest that the mechanisms determining chemical and electrical thresholds are by no means identical

(*d*) *Modification of seizure pattern* The seizures induced by supramaximal electrical stimulation in all laboratory animals and in man are characterized by the well-known sequence of tonic and clonic phases The rodents in particular show relatively little clonic activity, and the limbs are in extension throughout most of the tonic phase All of the effective anticonvulsants show some ability to modify this basic maximal seizure pattern (5 100), usually by abolishing the extensor component leaving a completely flexor tonic phase (100) Some agents in particular diphenylhydantoin, can abolish the tonic phase entirely leaving a clonic seizure of long duration This latter effect is also seen in human patients undergoing electroshock therapy (99) In laboratory animals the diphenylhydantoin-modified seizure is followed by a more rapid recovery of all central nervous functions (5) the evidence from post-seizure studies strongly suggests that the action of the drug occurs at all central nervous levels and is not selective for any center (101)

E Upon clinical convulsive disorders

Some clinical studies to be published in detail elsewhere (39) suggest that the beneficial effects of anticonvulsant medication upon convulsive disorders may be manifested in any or all of the following four different ways, short of complete remission

(*a*) *Reduction in frequency of seizures* This is the most usually recorded criterion of therapeutic benefit in the literature A modification in any of the presumptive mechanisms previously discussed might operate in the direction of reducing the number of attacks Seizure frequency data may be sometimes misleading particularly in disorders of the petit mal triad since an initial increase in frequency is often seen with ultimately effective therapy (40 61) All-or-none remissions and recurrences without gradations in frequency are also occasionally seen in petit mal.

(*b*) *Reduction in severity of seizures* Changes in the character of seizures are less frequently reported and more difficult to evaluate However, they are relatively common and sometimes indicate therapeutic benefit in the absence of reduction in seizure frequency Major seizures may be replaced by sensory attacks or confusion states of psychomotor type which previously occurred prodromally particularly with diphenylhydantoin therapy Petit mal attacks with motor manifestations (akinetic falling myoclonic jerking blepharospasm) may change to simple absences with Trimethadione therapy The change in severity may be attributable to the ability of the drug to reduce spread of convulsive activity from the primary focus to other areas.

(*c*) *Decrease in evocability of seizures* The increasing use of methods for "activating" the EEG or precipitating frank seizures should encourage further use of these procedures for evaluating therapy A dramatic example is the effect of Trimethadione upon the initiation of petit mal attacks by hyperventilation (40 59) Here it may be assumed that the principal action of the drug is to reduce the hypersensitivity of the primary focus.

(*d*) *Improvement in EEG* In the absence of clinical improvement an amelioration of EEG signs during treatment

sometimes correctly points the way to more adequate therapy The correlation between clinical and EEG improvement varies widely from patient to patient At one extreme are the frequent cases of complete suppression by Trimethadione of spike and wave discharges with concomitant freedom from seizures An intermediate group is found in which a diffuse dysrhythmia disappears under diphenylhydantoin treatment leaving a focal dysrhythmia which may previously have gone unnoticed Finally there are the occasional cases in which the focal or diffuse EEG signs continue unabated while the patient enjoys complete freedom from seizures *The latter effects like changes* in severity of seizures probably represent the ability of anticonvulsant drugs to prevent convulsive activation of normal areas by a primary focus

III THE SEARCH FOR MORE EFFECTIVE ANTIEPILEPTIC DRUGS

The most extensive studies on the relation between chemical structure and anticonvulsant activity have been those of Putnam and Merritt (69, 79) who used an electroshock seizure threshold test to determine anticonvulsant effectiveness

The author and his colleagues became convinced several years ago that no single laboratory method was adequate to reveal the several possible anticonvulsant properties of a given drug and therefore devised a battery of tests for scanning and assay of new agents (37 38 40 90 91 92 96) Four of these procedures have been retained for routine study and are described in detail elsewhere (91) Briefly the criteria of anticonvulsant action are

(*a*) Modification of maximal electroshock seizure pattern by abolition of tonic extensor component

(*b*) Elevation of normal electroshock seizure threshold,

(*c*) Prevention of lowering of electroshock seizure threshold in hydrated animals

(*d*) Protection against metrazol-induced seizures

The effective dose (ED_{50}) is calculated for a uniform end-point in each of the tests In addition a toxic dose level (TD_{50}) for production of minimal undesired central nervous signs (sedation ataxia etc) is also calculated The ED_{50} determinations are useful in comparing the relative anticonvulsant potencies of chemically related agents in order to observe the effects of structural modifications Since the potency of a substance is less important clinically than the relation between effective and toxic doses a Protective Index is derived for each of the four tests by dividing the TD_{50} by each of the ED_{50} values

These methods have been applied to a large number of drugs of which nine anticonvulsants of clinical value are compared here Figure 2 illustrates their common

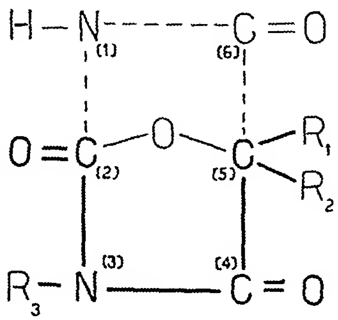


Fig 2 — Basic chemical structure of clinically useful antiepileptic drugs

Bold face Common denominator
Dash-line Barbiturate nucleus
Dotted line Hydantoin nucleus
Thin solid line Oxazolidine-2 4 dione nucleus
Opening of the hydantoin ring between positions 1 and 5 gives the corresponding acetylurea

chemical features Table II shows the effect of structural modification on relative potency as determined by the maximal seizure test Table III gives the protective indices obtained by all four assay procedures To facilitate comparison the results are represented graphically in figure 3 as profiles of action for one drug in each major chemical group

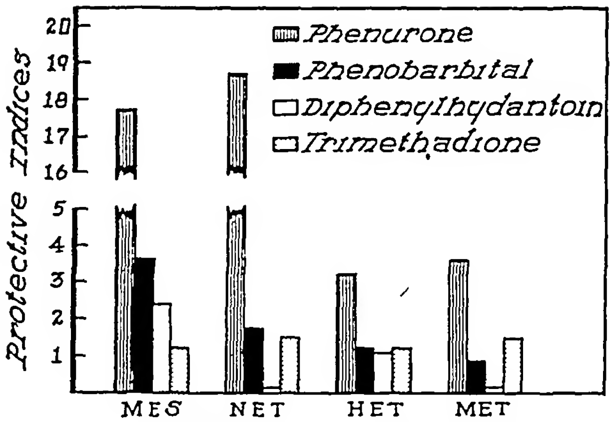


Fig 3 — Profiles of action of anticonvulsant drugs in rats

(Courtesy of E A SWINYARD (91))

M E S Maximal electroshock seizure test
N E T Normal electroshock threshold test
H E T Hydration electroshock threshold test
M E T Metrazol seizure test

Protective indices obtained by dividing toxic dose (TD_{50}) by effective dose (ED_{50}) as explained in text Note break in ordinate scale to accommodate high effectiveness of Phenurone

From the data it may be seen that the maximal seizure test gives a fair correlation with clinical efficacy against grand mal The results of this test on many drugs have been in substantial agreement with the evaluations of Merritt and Putnam (69) The metrazol index may have some limited predictive value for usefulness against petit mal While Phenurone is outstanding by all four protective indices, its absolute potency is not remarkable

In the search for more effective and less toxic agents several lines of investigation might be profitably extended Isotopic tracer studies on the metabolic fate of the more useful agents could yield valuable clues to effective degradation products A critical comparison of ring structures with their open-chain derivatives is especially in order (89) Solubility data and therapeutic blood level determinations are needed for those agents

Table II — Structure of some clinically effective antiepileptics, and their relative potency in modifying electroshock seizure pattern in rats

Antiepileptic [1]	*Structure* (See Fig 2)				*Potency* mg /kg ED_{50} ± SE
	Nucleus	R_1	R_2	R_3	
Mesantoin	Hydantoin	C_6H_5	C_2H_5	CH_3	4 52 ± 0 86
5-thienyl-5-phenyl hydantoin	Hydantoin	C_6H_5	C_4H_3S	H	16 8 ± 0 58
Diphenyl-hydantoin	Hydantoin	C_6H_5	C_6H_5	H	44 0 ± 2 82
Phenobarbital	Barbiturate	C_6H_5	C_2H_5	H	6 25 ± 0 32
Mebaral	Barbiturate	C_6H_5	C_2H	CH_3	15 5 ± 0 23
Trimethadione	Oxazolidine-2 4-dione	CH_3	CH	CH_3	360 ± 13 5
Paradione	Oxazolidine-2 4-dione	C_2H_5	CH_3	CH_3	238 ± 22 4
Epidon	Oxazolidine-2 4-dione	C_6H_5	C_6H_5	H	675 ± 88 0
Phenurone	Acetylurea	C_6H_5	H	H	41 2 ± 2 2

[1] Phenurone Trimethadione and Paradione were supplied by Abbott Laboratories Mebaral by Sterling Winthrop Mesantoin by Sandoz Chemical Works and 5-thienyl-5 phenyl hydantoin by Eli Lilly & Co

Table III — Protective indices of some clinically useful antiepileptic drugs by four different assay methods in rats

(Courtesy of E A SWINYARD (91))

Antiepileptic	$TD_{50} \pm SE$ mg /kg	PROTECTIVE INDICES ± SE (TD_{50}/ED_{50})			
		Maximal Electroshock Seizure Pattern	*Normal Electroshock Threshold*	*Hydration Electroshock Threshold*	*Metrazol Seizure Protection*
Mesantoin	50 ±3 1	11 1 ± 0 71	0 69 ± 0 07	1 42 ± 0 25	0 91 ± 0 08
5 thienyl-5-phenyl hydantoin	75 ± 6 5	4 46 ± 0 42	0	0 53 ± 0 05	0
Diphenyl-hydantoin	104 ± 8 0	2 36 ± 0 24	0	1 1 ± 0 09	0
Phenobarbital	22 ± 1 1	3 58 ± 0 26	1 75 ± 0 19	1 18 ± 0 12	0 85 ± 0 08
Mebaral	38 ± 1 1	2 46 ± 0 08	1 28 ± 0 20	2 04 ± 0 16	2 51 ± 0 18
Trimetha-dione	445 ± 27 7	1 23 ± 0 11	1 51 ± 0 17	1 17 ± 0 13	1 48 ± 0 13
Paradione	167 ± 11 5	0 7 ± 0 08	1 11 ± 0 10	1 05 ± 0 11	1 22 ± 0 14
Epidon	1200 ± 54 2	1 78 ± 0 25	1 00	1 00	0
Phenurone	730 ± 99 2	17 7 ± 2 60	18 7 ± 3 70	3 24 ± 0 72	3 65 ± 1 1

which are poorly water-soluble since required oral dosages may bear little relation to potency in solution (for example the high clinical dosage requirement and high margin of safety of Phenurone may be expressions of a fortuitously low solubility) A comparison of the isomeric forms of asymmetrical structures (e g Mesantoin) would be enlightening In the absence of an ideal all-purpose antiepileptic agent a more thorough analysis of drug combinations is needed for coupling greater effectiveness with attenuation of unwanted side-effects (56) More research is needed on the relation of chemical structure to the hematological dermatological and other toxic actions of otherwise useful agents

With such a manifold attack upon the pharmacology of anticonvulsant drugs it is within the realm of possibility that one or more ideal agents may be found which will suppress all seizure manifestations without impairment of central nervous function More probably the most effective agents in supratherapeutic dosage will be found to produce consistent central nervous signs since the neuronal properties which make seizures possible may also be essential in some manner for normal behavior In the long run, an adequate study of anticonvulsant action can be expected to cast new light on the mechanism of seizures and the converse is at least equally true

REFERENCES

1 ADRIAN E D and MORUZZI G Impulses in the pyramidal tract *J Physiol* 1939 *97* 153

2 ALBERTONI P Untersuchungen uber die Wirkung einiger Arzneimittel auf die Erregbarkeit des Grosshirns nebst Beitragen zur Therapie der Epilepsie *Arch f exper Path u Pharmakol* 1882 *15* 248

3 ALLES G A ELLIS C H FEIGEN G A and REDEMANN M A Comparative central depressant actions of some 5 phenyl 5 alkyl barbituric acids *J Pharmacol & Exper Therap* 1947 *89* 356

4 ARING C D and ROSENBAUM M Ingestion of large doses of dilantin sodium *Arch Neurol & Psychiat* 1941 *45* 265

5 BARANY E H and STEIN-JENSEN E The mode of action of anticonvulsant drugs on electrically induced convulsions in the rabbit *Arch internat de pharmacodyn et de therap* 1946 *73* 1

6 BELNAP W D TOMAN J E P and GOODMAN L S Tridione-diphenylhydantoin combination therapy in grand mal with slow-wave EEG dysrhythmia *Proc Fed Am Soc Exper Biol* 1947 *6* 308

7 BLUM E Die bekampfung epileptischer anfalle und ihrer folgeerscheinungen mit prominal *Deutsche med Wochnschr* 1932 *58* 696

8 BROOKS C McC and ECCLES J C An electrical hypothesis of central inhibition *Nature* 1947 *159* 760

9 BUBNOFF N and HEIDENHAIN R Uber erregungs- und hemmungsvorgange innerhalb der motorischen hirncentren *Pflügers Arch* 1881 *26* 137

10 CAHEN R L On the anticonvulsant activity of various nitrogen heterocycles I Alkylthioetherbarbiturates and II Phenylalkylthiomethylhydantoins *J Pharmacol & Exper Therap*, 1946, *88* 343

11 CHU N DRIVER R L HANZLIK P J Anticonvulsant action of isopropyl alcohol *J Pharmacol & Exper Therap* 1948 *92* 291

12 CLEIN N W New anticonvulsant in treatment of epilepsy 3-methyl 5,5-phenyl- ethylhydantoin (Hydantal) A preliminary report *Northwest Med* 1945 *44* 210

13 COHEN B and MYERSON A Mebaral in the treatment of epilepsy *New England J Med* 1942 *227* 336

14 DAVIDOFF E Tridione therapy in institutionalized epileptic patients *New York State J Med* 1947 *47* 1492

15 DAVIS J P and LENNOX W G The effect of trimethyloxazolidine dione and of dimethylethyloxazolidine dione on seizures and on the blood *Res Pub Ass nerv ment Dis* 1947 *26* 423

16 DEJONG R N Effect of tridione in the control of psychomotor attacks *J Am M A* 1946 *130* 565

17 DELAY J and SOULAIRAC A Comparative action of barbiturates hydantoins and bromides on electric epilepsy in the rat *Compt rend Soc de biol* 1944 *138* 60

18 DERCUM F X Luminal in epilepsy and in disturbed and excited states *J Nerv & Ment Dis* 1919 *50* 168

19 ELLERMANN M Experimental and clinical studies on the anticonvulsant properties of epidon *J Nerv & Ment Dis* 1947 *106* 369

20 ELLERMANN M Epidon — A new anti-epileptic *Nord Med* 1947 *35* 1541

21 EVERETT G M Anticonvulsant action of drugs against metrazol and anti-epileptic activity *Proc Fed Am Soc Exper Biol* 1946 *5* 26

21a EVERETT G M Pharmacological evaluation of anticonvulsant drugs (Presented before Am Br Internat League against Epilepsy, June 13 and 14, 1948)

22 EVERETT G M and RICHARDS R K Comparative anticonvulsive action of 3 5 5-trimethyloxazolidine-2 4-dione (tridione) dilantin and phenobarbital *J Pharmacol & Exper Therap* 1944 *81* 402

23 FABING H D, GAYLE R F and HAWKINS J R The treatment of epilepsy with sodium diphenylene hydantoin *Res Pub Ass nerv ment Dis* 1947 *26* 398

24 FINKELMAN I and ARIEFF A J Untoward effects of phenytoin sodium in epilepsy *J Am M A* 1942 *118* 1209

25 FREYHAN F A Effectiveness of diphenylhydantoin in management of non-epileptic psychomotor excitement states *Arch Neurol & Psychiat* 1945 *53* 370

26 FROST I Sodium diphenyl hydantoin in the treatment of epilepsy preliminary observations in severe cases *J Ment Sc* 1939 *85* 976

27 GIBBS E L and GIBBS F A Diagnostic and localizing value of electro-encephalographic studies in sleep *Res Pub Ass nerv ment Dis* 1947 *26* 366

28 GIBBS F A New drugs of value in the treatment of epilepsy *Ann Int Med* 1947 *27* 548

29 GIBBS F A, EVERETT G M and RICHARDS R K Phenurone in epilepsy (Presented before Am Br Internat League against Epilepsy, June 13 and 14 1948)

30 GLEY P FOURNIER P and TOUCHARD T Action de la diphenylhydantoine et de l ethylphenyl malonylurea sur l epilepsie souscorticale *Compt rend Soc de biol* 1945 *139* 298

31 GLEY P LAPIPE M RONDEPIERRE J HORANDE H and TOUCHARD T Action des antepileptiques sur les convulsions electriques medullaires *Compt rend Soc de biol* 1944 *138* 231

32 GOLDSTEIN H H and WEINBERG J Experimental evidence of anticonvulsant properties of sodium diphenyl hydantoinate (dilantin sodium N N R) *Arch Neurol & Psychiat* 1940 *43* 453

33 GOODMAN L and LIH B Effect of dilantin on metrazol convulsions *J Pharmacol & Exper Therap* 1941 *72* 18

34 GOODMAN L and MANUEL C The anticonvulsant properties of dimethyl-N-methylbarbituric acid and 3 5 5-trimethyloxazolidine-2 4-dione (tridione) *Proc Fed Am Soc Exper Biol* 1945 *4* 119

35 GOODMAN L S SWINYARD E A and TOMAN, J E P Studies on the anticonvulsant properties of diphenylhydantoin *Proc Fed Am Soc Exper Biol* 1946 *5* 180

36 GOODMAN L S SWINYARD E A and TOMAN J E P Anticonvulsant properties of 5 5-phenyl thienyl hydantoin in comparison with dilantin and mesantoin *Proc Soc Exper Biol Med* 1948 *68* 584

37 GOODMAN L and TOMAN J E P Experimental indices for comparing the efficacy of compounds with anticonvulsant and antiepileptic properties *Proc Fed Am Soc Exper Biol* 1945 *4* 120

38 GOODMAN L S and TOMAN J E P Anticonvulsants physiological and pharmacological background and methods of evaluation *Proc First Nat Medicinal Chemistry Symp of the Am Chem Soc*, 1948 *June 17-19* 93

39 GOODMAN L S and TOMAN J E P (unpublished observations)

40 GOODMAN L S TOMAN J E P and SWINYARD E A The anticonvulsant properties of tridione

Laboratory and clinical investigations *Am J Med* 1946 *1* 213

41 GRINKER J Further experience with phenobarbital (luminal) in epilepsy *J Am M A* 1920 *75* 588

42 GRUBER C M HAURY V G and DRAKE M E The toxic action of sodium diphenylhydantoinate (dilantin) when injected intraperitoneally and intravenously in experimental animals *J Pharm Exper Therap* 1940 *68* 433

43 GUTIERREZ NORIEGA C Action of metrazol on the motor and sensory nuclei of the brain stem *J Neuropath & Exper Neurol* 1943 *2* 132

44 GUTIERREZ-NORIEGA C Biologie et physiologie des convulsions epileptiques *Scientia* 1947 May-June 38

45 HAUPTMANN A Luminal bei Epilepsie *München med Wochnschr*, 1912 *59* 1907

46 HEMPHILL R E and WALTER W G Epanutin and electric convulsion therapy *Lancet* 1941 *240* 446

47 HEYDE W Uber Prominal und Luminalwirkung bei Schweren epileptischen Erkrankungen *Klin Wochnschr* 1932 *11* 1874

48 IMPENS E Pharmakologisches uber luminal oder phenylathylbarbitursaure *Deutche med Wochnschr* 1912 *38* 945

49 JACKSON J H Selected writings of John Hughlings Jackson Volume I (Edited by James Taylor) Hodder and Stoughton London 1931

50 JASPER H H and DROOGLEEVER-FORTUYN J Experimental studies on the functional anatomy of petit mal epilepsy *Res Pub Ass nerv ment Dis* 1947 *26* 272

51 JULIUSBURGER O Uber Luminal ein neues hypnoticum und sedativum *Berl klin Wochnschr* 1912 *49* 940

52 KALINOWSKY L B Convulsions in nonepileptic patients on withdrawal of barbiturates alcohol and other drugs *Arch Neurol & Psychiat* 1942 *48* 946

53 KALINOWSKY L B and KENNEDY F Observations in electric shock therapy applied to problems of epilepsy *J Nerv & Ment Dis* 1943 *98* 56

54 KELLER A D and FULTON J F The action of anesthesic drugs on the motor cortex of monkeys *Am J Physiol* 1931 *97* 537

55 KNOEFEL P K and LEHMANN G The anticonvulsant action of diphenyl hydantoin and some related compounds *J Pharm Exper Therap* 1942 *76* 194

56 KOZOL H L Epilepsy treatment with new drug 3 methyl 5 5 phenyl ethyl-hydantoin (phenantoin) *Am J Psychiat* 1946 *103* 154

57 LENNOX W G The petit mal epilepsies — their treatment with tridione *J Am M A* 1945 *129* 1069

58 LENNOX W G The treatment of epilepsy *Med Clinics of North America* 1945 *29* 1114

59 LENNOX W G Newer agents in the treatment of epilepsy *J Pediat* 1946 *29* 356

60 LENNOX W G Tridione in the treatment of epilepsy *J Am M A* 1947 *134* 138

61 LENNOX W G and COBB S Studies in epilepsy VIII The clinical effect of fasting *Arch Neurol & Psychiat* 1928 *20* 771

62 LOCOCK C (Discussion of paper by E H Sieveking) *Lancet* 1857 *1* 527

63 LOEWE S Klinische erfahrungen mit luminal *Deutsche med Wochnschr* 1912 *42* 947

64 LOSCALZO A E Treatment of epileptic patients with a combination of 3 methyl 5 5 phenylethylhydantoin and phenobarbital Preliminary report *J Nerv & Ment Dis* 1945 *101* 537

65 MARBURG O and HELFAND M Analysis of one hundred cases of epilepsy *J Nerv & Ment Dis* 1946 *104* 465

66 MERRITT H H and BRENNER C Studies in new anticonvulsants *Bull New York Acad Med* 1947, *23* 292

67 MERRITT H H and PUTNAM T J A new series of anticonvulsant drugs tested by experiments on animals *Arch Neurol & Psychiat* 1938 *39* 1003

68 MERRITT H H and PUTNAM T J Sodium diphenyl hydantoinate in treatment of convulsive seizures *Arch Neurol & Psychiat* 1939 *42* 1053

69 MERRITT, H H and PUTNAM T J Experimental determination of anticonvulsive activity of chemical compounds *Epilepsia* 1945 *3* 51

70 MILLMAN C G Luminal and prominal in epilepsy *Brit M J* 1937 *2* 61

71 MOORE M T Symptomatic abdominal epilepsy *Am J Surg* 1946 *72* 883

72 MORUZZI G L Epilessia Sperimentale Monograph Nicola Zanichelli (Editor) Bologna 1946

73 PENFIELD W and HUMPHREYS S Epileptogenic lesions of the brain A histologic study *Arch Neurol & Psychiat* 1940 *43* 240

74 PENFIELD W and JASPER H Highest level seizures *Res Pub Ass nerv ment Dis* 1947 *26* 252

75 PERLSTEIN M A and ANDELMAN M B Tridione its use in convulsive and related disorders *J Pediat* 1946 *29* 20

76 PETERMAN M G Convulsions in childhood *South M J* 1948 *41* 62

77 PFEIFFER C C A rapid experimental method for screening anticonvulsant substances (Presented before Am Br Internat League Against Epilepsy June 13-14 1948)

78 PUTNAM T J and MERRITT H H Experimental determination of the anticonvulsant properties of some phenyl derivatives *Science* 1937 *85* 525

79 PUTNAM T J and MERRITT H H Chemistry of anticonvulsant drugs *Arch Neurol & Psychiat* 1941 *45* 505

80 PUTNAM T J and MERRITT H H Dulness as an epileptic equivalent *Arch Neurol & Psychiat* 1941 *45* 797

81 RICHARDS R K EVERETT G M and PICKRELL K L Pharmacological and clinical studies of tridione with special reference to its analgesic action *Anesth and Analges* 1946 *25* 147

82 RICHARDS R K and PERLSTEIN M A Tridione a new drug for the treatment of convulsive and re

lated disorders *Arch Neurol & Psychiat*, **1946** *55* 164

83 ROSENBLUETH, A and CANNON W B Cortical responses to electric stimulation *Am J Physiol* **1942** *135* 690

84 SANDS D E The treatment of epilepsy with psychosis by prominal *J Ment Dis* **1937** *83* 702

85 SCHUTZ F Serum choline esterase in barbiturate addiction and epilepsy *Quart J Exper Physiol* **1944** *33* 35

86 SHERRINGTON, C S The integrative action of the nervous system Yale University Press, New Haven, Conn, **1906**

87 SLOAN L L and GILGER A P Visual effects of tridione *Am J Ophth* **1947** *30* 1387

88 SPIELMAN, M A Some analgesic agents derived from oxazolidine 2-4 dione *J Am Chem Soc* **1944** *66* 1244

89 SPIELMAN, M A Some anticonvulsants *Proc First Nat Medicinal Chemistry Symp of the Am Chem Soc* **1948** June 17-19 119

90 SWINYARD E A Validity of laboratory anticonvulsant tests for predicting antiepileptic potency and specificity *Proc Fed Am Soc Exper Biol*, **1947**, *6* 376

91 SWINYARD E A Laboratory assay of clinically effective antiepileptic drugs *J Am Pharm Assoc*, **1949** (Sci Ed) In press

92 SWINYARD E A and GOODMAN L S Laboratory assay of anticonvulsant potency of some hydantoinates *Proc Fed Am Soc Exper Biol* **1946** *5* 205

93 SWINYARD E A TOMAN J E P and GOODMAN L S The effect of cellular hydration on experimental electroshock convulsions *J Neurophysiol* **1946** *9* 47

94 TAINTER M L TAINTER E G, LAWRENCE W S NEURU E N LACKEY R W LUDUENA F P KIRTLAND H B and GONZALES R I Influence of various drugs on the threshold for electrical convulsions *J Pharmacol & Exper Therap* **1943**, *79* 42

95 THORNE, F C The anticonvulsant action of tridione *Psychiat Quart* **1945** *19* 686

96 TOMAN J E P and GOODMAN L S Conditions modifying convulsions in animals *Res Pub Ass nerv ment Dis*, **1947** *26* 141

97 TOMAN J E P and GOODMAN, L S Anticonvulsants *Physiol Rev* **1948** *28* 409

98 TOMAN J E P and HENDLEY C D A comparison of action of anticonvulsants on the excitability of peripheral nerve and the motor cortex **1949** (To be published)

99 TOMAN J E P, LOEWE, S and GOODMAN, L S Studies on the physiology and therapy of convulsive disorders I The effect of anticonvulsant drugs on electroshock seizures in man *Arch Neurol & Psychiat* **1947** *58* 312

100 TOMAN J E P, SWINYARD E A and GOODMAN, L S Properties of maximal seizures, and their alteration by anticonvulsant drugs and other agents *J Neurophysiol* **1946** *9* 231

101 TOMAN J E P WOODBURY J W, SIMONS, J, EVANS R and BURTON T Y Effect of diphenylhydantoin on recovery of various central nervous functions following maximal electroshock seizures in cats **1949** (To be published)

102 WALKER, C F and KIRKPATRICK, B B Dilantin treatment for behavior problem children with abnormal electroencephalograms *Am J Psychiat* **1947**, *103* 484

103 WEESE H Zur Pharmacologie des Prominal *Deutsche med Wochnschr* **1932**, *58* 696

104 WILKS S Observations on the pathology of some of the diseases of the nervous system *Guy's Hosp Rep* **1866** *12* 152

105 ZISKIND E SJAARDEMA H and BERCEL, N A Minimal electroencephalographic response to metrazol as a method for measuring the convulsive threshold for use in human beings *Science* **1946** *104* 2707

INFLUENCE OF DRUGS ON THE HUMAN ELECTROENCEPHALOGRAM [1]

William G Lennox, M D

Electroencephalography is only nineteen years of age The thrill of watching the brain write its own confession of guilt on moving paper is not yet lost Description of changes in the frequency and height of surface waves in relationship to clinical symptoms is of practical value, but we must not stop there For unnumbered generations men have watched the ocean waves but the science of oceanography — the study of forces behind the wave and the current — is only beginning This morning our minds have been swept by the salty winds of discovery We sense an approach to the meaning and the origin of the electrical activity of the nervous system Great significance attaches to the studies of Dr Toman and his associates and their analysis of the action of certain anticonvulsants on electrical phenomena My discussion will be relatively superficial and limited to clinical observations

Dysrhythmia pharmacology and epilepsy form a triangle of mutual interest and dependence We may view these relationships in order First pharmacology and seizures second, seizures and dysrhythmia, third dysrhythmia and pharmacology, and finally the inter-relationships of these three

PHARMACOLOGY AND SEIZURES

A measure of seizure control has been possible for the past 91 years nevertheless little is known about the mechanism of drug therapy and certain misconceptions have hindered progress

First is the presumption that an anticonvulsant must necessarily be a sedative True the first successful remedy bromide was a sedative although it was first used not for that reason but because it caused impotence The use of repressants seemed to be justified by the strong voice of Hughlings Jackson proclaiming that involuntary muscle movements mean an excessive discharge of nervous elements However there is the contrary theory of release of movement from failure of discharge of inhibiting centers Also some seizures consist of failure of muscle movement The ancients made use of mild stimulants but only in the last decade has the value of non-sedatives or stimulants such as diphenyl hydantoin trimethyloxazolidine dione phenacetylurea (phenurone), caffeine amphetamine sulphate and glutamic acid been demonstrated Potentially all the drawers of the medicine chest are now open to us and not just the one marked Sedation

However discovery of an effective drug by the method of trial and error by using everything in sight — first on animals and then on patients — is slow and uncertain All praise to Merritt (1) and his associates in their laborious screening of 700 chemicals a labor that yielded a diphenyl hydantoin Now we sense the beginning of a more rational approach the building of a chemical structure that will meet a given symptom A preview of this approach is the paper by Richards A New Mechanism of Anticonvulsive Activity in the program of the American League Against Epilepsy

A second misconception is that any antiepileptic is equally effective for all sorts of epileptic seizures This thought is the natural result of having but one effective medicine — first bromide and then phenobarbital for a period of 80 years or for three generations of medical practice Recent drugs that have come through the screen of animals and patients demonstrate that a given type of seizure will respond best to a given drug For example trimethyloxazolidine dione is effective in the control of petit mal but not of convulsions dilantin helps convulsive sei-

[1] From the Children s Medical Center, Boston and the Department of Neurology of the Harvard Medical School No LIV in a series *Studies in Epilepsy*